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Mobile phone-based interventions for improving adherence to medication prescribed for the primary prevention of cardiovascular disease in adults (Review)

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[Intervention Review]

Mobile phone-based interventions for improving adherence to medication prescribed for the primary prevention of cardiovascular disease in adults

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ABSTRACT

Background

Cardiovascular disease (CVD) is a major cause of disability and mortality globally. Premature fatal and non-fatal CVD is considered to be largely preventable through the control of risk factors by lifestyle modifications and preventive medication. Lipid-lowering and antihypertensive drug therapies for primary prevention are cost-effective in reducing CVD morbidity and mortality among high-risk people and are recommended by international guidelines. However, adherence to medication prescribed for the prevention of CVD can be poor. Approximately 9% of CVD cases in the EU are attributed to poor adherence to vascular medications. Low-cost, scalable interventions to improve adherence to medications for the primary prevention of CVD have potential to reduce morbidity, mortality and healthcare costs associated with CVD.

Objectives

To establish the effectiveness of interventions delivered by mobile phone to improve adherence to medication prescribed for the primary prevention of CVD in adults.

Search methods

We searched CENTRAL, MEDLINE, Embase, and two other databases on 7 January 2020. We also searched two clinical trials registers on 5 February 2020. We searched reference lists of relevant papers. We applied no language or date restrictions.

Selection criteria

We included randomised controlled trials investigating interventions delivered wholly or partly by mobile phones to improve adherence to cardiovascular medications prescribed for the primary prevention of CVD. We only included trials with a minimum of one-year follow-up in order that the outcome measures related to longer-term, sustained medication adherence behaviours and outcomes. Eligible comparators were usual care or control groups receiving no mobile phone-delivered component of the intervention.

Data collection and analysis

We used standard methodological procedures recommended by Cochrane. The main outcomes of interest were objective measures of medication adherence (blood pressure (BP) and cholesterol), CVD events, and adverse events. We contacted study authors for further information when this was not reported.

Main results

We included 14 trials with 25,633 randomised participants. Participants were recruited from community-based primary and tertiary care or outpatient clinics. The interventions varied widely from those delivered solely through short messaging service (SMS) to those involving a combination of modes of delivery, such as SMS in addition to healthcare worker training, face-to-face counselling, electronic pillboxes, written materials, and home blood pressure monitors. Some interventions only targeted medication adherence, while others additionally targeted lifestyle changes such as diet and exercise. Due to heterogeneity in the nature and delivery of the interventions and study populations, we reported most results narratively, with the exception of two trials which were similar enough to meaningfully pool in meta-analyses.

The body of evidence for the effect of mobile phone-based interventions on objective outcomes of adherence (BP and cholesterol) was of low certainty, due to most trials being at high risk of bias, and inconsistency in outcome effects. Two trials were at low risk of bias.

Among five trials (total study enrolment: 5441 participants) recording low-density lipoprotein cholesterol (LDL-C), two studies found evidence for a small beneficial intervention effect on reducing LDL-C (−5.30 mg/dL, 95% confidence interval (CI) −8.30 to −2.30; and −9.20 mg/dL, 95% CI −17.70 to −0.70). The other three studies found results varying from a small reduction (−7.7 mg/dL) to a small increase in LDL-C (0.77 mg/dL). All of which had wide confidence intervals that included no effect.

Across 13 studies (25,166 participants) measuring systolic blood pressure, effect estimates ranged from a large reduction (MD −12.45 mmHg, 95% CI −15.02 to −9.88) to a small increase (MD 2.80 mmHg, 95% CI 0.30 to 5.30). We found a similar range of effect estimates for diastolic BP, ranging from −12.23 mmHg (95% CI −14.03 to −10.43) to 1.64 mmHg (95% CI −0.55 to 3.83) (11 trials, 19,716 participants). Four trials showed intervention benefits for systolic and diastolic BP with confidence intervals excluding no effect, and among these were all three of the trials evaluating self-monitoring of blood pressure with mobile phone-based telemedicine. The fourth trial included SMS and provider support (with additional varied features). Seven studies (19,185 participants) reported 'controlled' BP as an outcome, and intervention effect estimates varied from negligible effects (odds ratio (OR) 1.01, 95% CI 0.76 to 1.34) to large improvements in BP control (OR 2.41, 95% CI: 1.57 to 3.68). The three trials of clinician training or decision support combined with SMS (with additional varied features) had confidence intervals encompassing benefits and harms, with point estimates close to zero. Pooled analyses of the two trials of interventions solely delivered through SMS were indicative of little or no beneficial intervention effect on systolic BP (MD −1.55 mmHg, 95% CI −3.36 to 0.25; I^2 = 0%) and small increases in controlled BP (OR 1.32, 95% CI 1.06 to 1.65; I^2 = 0%).

Based on four studies (12,439 participants), there was very low-certainty evidence (downgraded twice for imprecision and once for risk of bias) relating to the intervention effect on combined (fatal and non-fatal) CVD events.

Two studies (2535 participants) provided low-certainty evidence for the effect of the intervention on cognitive outcomes, with little or no difference between trial arms for perceived quality of care and satisfaction with treatment.

There was moderate-certainty evidence (downgraded due to risk of bias) that the interventions did not cause harm, based on six studies (8285 participants). Three studies reported no adverse events attributable to the intervention. One study reported no difference between groups in experience of adverse effects of statins, and that no participants reported intervention-related adverse events. One study stated that potential side effects were similar between groups. One study reported a similar number of deaths in each arm, but did not provide further information relating to potential adverse events.

Authors' conclusions

There is low-certainty evidence on the effects of mobile phone-delivered interventions to increase adherence to medication prescribed for the primary prevention of CVD. Trials of BP self-monitoring with mobile-phone telemedicine support reported modest benefits. One trial at low risk of bias reported modest reductions in LDL cholesterol but no benefits for BP. There is moderate-certainty evidence that these interventions do not result in harm. Further trials of these interventions are warranted.

PLAIN LANGUAGE SUMMARY

Interventions delivered by mobile phone to help people adhere to medication to prevent heart and circulatory disease

Review question

We reviewed the evidence on the effect of interventions delivered by mobile phone to help people in taking their medication to prevent cardiovascular disease (for example, heart attacks and strokes).

Background

Around 17.6 million people die from cardiovascular disease every year. Medications can help to prevent cardiovascular disease, but many people who have been given these medications do not take them as often or as consistently as recommended. This means that the medication will not work as well as it could to prevent cardiovascular disease. Interventions delivered through mobile phones, for example, prompting by text messaging, may be a low-cost way to help people to take their medication as recommended.

Study characteristics

The evidence is up to date to January 2020. We found 14 studies that tested interventions delivered at least partly by mobile phone, which followed up participants for at least 12 months.

Key results

We were not able to combine the results of most of the trials, because the interventions were very different. Two studies were at low risk of bias and 12 were at high risk of bias. The effects of the interventions were inconsistent across studies, and so we are not confident about their findings. Self-monitoring of blood pressure plus telemedicine support by mobile phone may improve blood pressure control, but we are not confident about the findings due to trials being at risk of bias. Interventions delivered by text message alone may have little or no effect on blood pressure control. Interventions which included text messages and clinician training or clinician decision support (with or without additional features) may have little or no effect on blood pressure or cholesterol. The effects of the interventions which included text messages and provider support (with or without other features) were inconsistent across studies, and so we are not confident about their findings. We are uncertain about the effects of apps held by the patient or apps with additional provider support. Some interventions delivered by mobile phone may help people to take their medication, but the benefits are small or modest. Some trials found that the interventions did not have any beneficial effect. There was no evidence to suggest that these types of interventions caused harm.

SUMMARY OF FINDINGS

Summary of findings 1. Mobile phone interventions compared to usual care for improving adherence to medication prescribed for primary prevention of cardiovascular disease

Mobile phone interventions compared to usual care for improving adherence to medication prescribed for primary prevention of cardiovascular disease

Patient or population: people prescribed medication for primary prevention of cardiovascular disease
Setting: community and healthcare settings
Intervention: mobile phone-based interventions
Comparison: usual care, passive text messages, or 'enhanced' usual care

Outcomes	Impact	№ of participants[f] (studies)	Certainty of the evidence (GRADE)
Objective measure of medication adherence: Cholesterol (low-density lipoprotein) follow-up: range 1 – 2 years	2 studies found evidence of a small beneficial intervention effect on reducing LDL-C (−9.20 mg/dL, and 5.3 mg/dL), and 3 studies found results varying from a small reduction (−7.7 mg/dL) to a small increase in LDL-C (0.77 mg/dL), all of which had wide confidence intervals that included no effect.	5,441 (5 RCTs)	⊕⊕⊖⊖ **Low** [a,b]
Objective measure of medication adherence: Blood pressure follow-up: range 1 – 2 years	Systolic BP: 9 of 13 studies found lower systolic blood pressure with mobile-phone interventions, although only 4 of these reductions in systolic blood pressure had confidence intervals excluding no effect. Across the 13 studies, effect estimates varied greatly, from those showing a large reduction (−12.45 mmHg) to those reporting a small increase (+2.80 mmHg) in systolic blood pressure. Meta-analysis of 2 trials evaluating an intervention targeting adherence to blood pressure medication delivered solely by SMS messaging provided a pooled MD of −1.55 mmHg, 95% CI −3.36 to 0.25.	25,166 (13 RCTs)	⊕⊕⊖⊖ **Low** [a,b]
	Diastolic BP: 8 of 11 studies found lower diastolic blood pressure with mobile-phone interventions, but in 4 of these the confidence intervals included no effect. Across the 11 studies, effect estimates varied widely from those showing a large reduction (−12.23 mmHg) to those showing a small increase (+1.64 mmHg) in diastolic blood pressure.	19,716 (11 RCTs)	
	Controlled BP: 7 studies reported 'controlled' blood pressure as an outcome, of which six reported increased blood pressure control with mobile phone interventions, although in only one of these studies did the confidence interval exclude no effect. Effect estimates varied from negligible (OR 1.01) to large improvements in blood pressure control (OR 2.41). Meta-analysis of 2 trials evaluating an intervention targeting adherence to blood-pressure medication delivered solely by SMS messaging indicated a modest beneficial intervention effect: pooled OR of 1.32, 95% CI 1.06 to 1.65.	19,185 (7 RCTs)	
Combined CVD events	1 trial reported on deaths due to CVD, and 3 recorded non-fatal CVD events. For 3 studies the effect estimate was in the direction of harm, and for the 4th it was in the direction of interven-	12,439 (4 RCTs)	⊕⊖⊖⊖ **Very low** [c, d]

	tion benefit. However, the number of events in each trial was low and all effect estimates had wide 95% confidence intervals encompassing no effect.		
Adverse events follow-up: range 1 – 2 years	3 studies reported that there were no adverse events attributable to the intervention. 1 reported that there was no difference between groups in adverse effects of statins, and that no participants reported intervention-related adverse events. 1 study reported that potential side effects were similar between groups. 1 study reported a similar number of deaths in the intervention and control arms, but did not provide further information relating to potential adverse events.	8285 (6 RCTs)	⊕⊕⊕⊖ **Moderate** [b]
Cognitive outcome: satisfaction with treatment follow-up: mean 1 year	1 study measured satisfaction with treatment, and found no evidence of a difference between intervention and control arms. 1 study reported on perceived quality of care, with little difference observed between the 2 groups.	2535 (2 RCT)	⊕⊕⊖⊖ **Low** [d,e]

LDL-C: low-density lipoprotein cholesterol; BP: blood pressure; RCT: randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level for inconsistency: trial results included large variations in the degree to which the outcome was affected.
[b]Downgraded one level for risk of bias: most trials at unclear risk of bias for multiple domains.
[c] Downgraded two levels for imprecision: very few events and wide confidence intervals encompassing intervention benefit and harm.
[d]Downgraded one level for risk of bias: trials at unclear or high risk of bias for several domains.
[e]Downgraded one level for indirectness: based on two trials, one conducted in public sector clinic in Cape Town, South Africa, and one in community health settings in India.
[f] Total study enrolment.

BACKGROUND

Description of the condition

Cardiovascular disease (CVD) is a major cause of disability and mortality throughout the world (Roth 2018; WHO 2011; WHO 2016), with an estimated 17.8 million people dying from CVDs in 2017, accounting for almost a third of all global deaths (Roth 2018). However, premature fatal and non-fatal CVD is considered to be largely preventable through the control of risk factors (WHO 2011).

Primary prevention of CVD refers to actions taken to reduce the incidence of clinical events due to coronary heart disease (CHD), cerebrovascular disease and peripheral vascular disease, among people with risk factors who have not yet developed clinically-manifest CVD (WHO 2007). Primary prevention of CVD consists of lifestyle modifications (e.g. smoking cessation, increasing physical activity) and drug therapy (Piepoli 2016).

Lipid-lowering and antihypertensive drug therapies for primary prevention are cost-effective in reducing CVD morbidity and mortality among high-risk people and are recommended by international guidelines (Piepoli 2016; WHO 2007). Recommendations relating to the use of antiplatelet drugs for primary prevention vary. The European Society of Cardiology (ESC) states that aspirin cannot be recommended in primary prevention due to its increased risk of major bleeding (Piepoli 2016); however, the US Preventive Services Task Force (USPSTF) recommends the use of aspirin when the 10-year risk of CVD events reaches such a level that the benefits of aspirin, in terms of CVD events prevented, outweigh the potential harm of increased gastrointestinal haemorrhage (USPSTF 2014).

Adherence to long-term medication is not ideal and results in costs in both health and economic terms (Piepoli 2016). Meta-analyses have estimated rates of adherence to cardiovascular medications ranging from 50% to 60% (Chowdhury 2013; Naderi 2012), and there is some evidence that adherence is lower for primary prevention (Naderi 2012).

One study of health records of over 430,000 people in UK general practices found that 47% of people prescribed statins for primary prevention discontinued treatment (indicated by a greater than 90-day gap between prescriptions). Among these people, 72% then restarted treatment (Vinogradova 2016). One study of Finnish healthcare registers found that 53% of women prescribed statin therapy for primary prevention were adherent (defined as exceeding 80% of the prescribed regimen) (Lavikainen 2016). It has been estimated that approximately 9% of cases of CVDs in the EU could be attributed to poor adherence to vascular medications (Chowdhury 2013). Improving adherence to medications for the primary prevention of CVD would help to maximise the clinical benefits for the wider population (WHO 2003). There is therefore considerable scope for increasing adherence to prescribed medicine, and thereby reducing morbidity, mortality and healthcare costs.

Description of the intervention

Mobile phone ownership is almost universal in high-income countries and estimated to have reached over 90% in low- and middle-income countries (ICT 2016). Given the broad reach of mobile phones and the potential for automation of delivery, interventions delivered by mobile phone are a potentially cost-effective strategy to improve medication adherence. A range of media can be delivered through mobile phones, including text messages, picture messages, interactive-voice response, telephone calls and, with increasing ownership of smart phones with Internet capabilities (ICT 2016), mobile applications.

How the intervention might work

A wide range of factors have been shown to be associated with medication non-adherence (DiMatteo 2004; Julius 2009; Kardas 2013; Pound 2005; Vermeire 2001; WHO 2003). Mobile phone-based interventions have the potential to target a number of these factors. For example, lack of adherence resulting from lack of information about the benefits of medication, lack of information about how they work and how to take them, misconceptions about medication adverse effects, complex or unclear advice or poor recall of information provided in consultations may be addressed through text messages providing short and simply-worded snippets of information (Julius 2009; Kardas 2013; Pound 2005; Vermeire 2001). Experiences of adverse effects can be targeted through mobile phone-delivered interventions by providing information about medication and facilitating a link to a healthcare professional for people experiencing problems with their medication. Lack of social support has also been linked to poor medication adherence; previous qualitative research found that the receipt of text message-based intervention provided social support (Douglas 2013). Mobile phone-delivered interventions can be designed to target psychological factors such as lack of motivation and low self-efficacy (Free 2016).

Existing interventions targeting adherence to CVD medication have employed mobile technologies to: deliver medication reminders (Park 2014a); encourage self-monitoring of medication intake (Park 2014a); encourage habit formation relating to medication-taking behaviours (Bobrow 2014); provide information (Bobrow 2014; Park 2014a); and facilitate links to healthcare services where required (Bobrow 2014; Piette 2012).

Systematic reviews assessing the effect of mobile health (mhealth) interventions on medication adherence for a range of conditions, including HIV, non-communicable diseases and prevention of transplant rejection have reported significant improvements (Anglada-Martinez 2015; Park 2014b). An RCT has found mobile phone messaging to be effective in improving contraceptive use (Smith 2015). Few adverse effects of mobile phone-based interventions have been reported; potential, but rare, adverse events may include road traffic accidents (Caird 2014).

Why it is important to do this review

Systematic reviews evaluating the effect of mhealth interventions have reported promising but inconclusive results about improved medication adherence, including adherence to medication for secondary prevention of heart disease (Adler 2017; Anglada-Martinez 2015; Park 2014b). However, no systematic review has specifically examined the effect of mobile phone-based interventions on adherence to medications for the *primary* prevention of CVD. Mobile phone-based interventions are of particular interest, given their low cost and potential for widespread delivery.

OBJECTIVES

To establish the effectiveness of interventions delivered by mobile phone to improve adherence to medication prescribed for the primary prevention of CVD in adults.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) of parallel-group design that randomised by participant or by cluster. We did not include cross-over trials, as this design would be inappropriate for assessing effects on cardiovascular events or mortality, due to the irreversible nature of these events. We only included trials with a minimum of one-year follow-up in order that the outcome measures relate to longer-term, sustained medication adherence behaviours and outcomes. We included studies published as full text and as abstract only, and unpublished data.

Types of participants

We included adults (aged 18 years and over) who have been prescribed medication for the primary prevention of CVD. As this review focuses on the primary prevention of CVD, we only included studies involving participants who had not had a prior CVD event, defined as: a previous myocardial infarction, stroke, revascularisation procedure (coronary artery bypass grafting or percutaneous coronary intervention), people with angina, and people with angiographically-defined CHD. Where we identified trials that included a subset of eligible participants, we contacted the authors to request data for only those participants of interest. When we were unable to access these data, we applied a cut-off which included only trials in which at least 75% of participants met the criteria for primary prevention.

Types of interventions

We included trials of interventions delivered wholly or partly by mobile phone to improve adherence to cardiovascular medications prescribed for the primary prevention of CVD. We included interventions targeting adherence to antihypertensive drugs (thiazide-like diuretic, angiotensin-converting enzyme inhibitor, calcium channel blocker, beta-blocker); lipid-lowering drugs (statins); and antiplatelet drugs (low-dose aspirin, non-aspirin antiplatelet drugs). We only included trials targeting adherence to at least one of these medications. We also included trials of interventions that targeted medication adherence alongside other lifestyle modifications.

Intervention

Any mobile phone-specific delivery mechanism, including short messaging service (SMS), multimedia messaging (MMS), applications (apps) and Interactive Voice Response. We included interventions employing a mix of delivery mechanisms of which at least one was mobile phone-based, for example, interventions delivered by mobile phones in combination with traditional methods such as face-to-face communication and links to other types of support (e.g. healthcare support worker, telephone calls, Internet pages).

Comparator

Usual care and active controls, where the control group intervention had no component delivered by a mobile phone-specific delivery mechanism.

Types of outcome measures

Reporting one or more of the outcomes listed here in the trial was not an inclusion criterion for the review.

Where outcomes (primary or secondary) were measured at multiple time points, we extracted data for the final point of measurement.

Primary outcomes

- Objective measures of adherence to treatment (low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C), for the effect of statins; blood pressure for antihypertensive drugs; heart rate for the effect of atenolol; urinary 11-dehydrothromboxane B2 for the antiplatelet effects of aspirin).
- Combined CVD events (fatal or non-fatal events).
- Adverse effects including self-reported road traffic accidents.

Secondary outcomes

- Indirect measures of adherence to treatment (self-report, tablet counts, medication event monitoring systems, pharmacy prescription data).
- Fatal cardiovascular events.
- Non-fatal cardiovascular events (CHD, stroke).
- Health-related quality of life assessed using validated instruments (e.g. 36-Item Short Form Health Survey (SF-36), EQ-5D).
- Cognitive outcomes (any measures of: satisfaction with treatment, medication-taking self-efficacy, autonomy related to medication, attitudes (e.g. concerns about medicine adverse effects)).
- Costs.

We also reported on the following process measures: extent of intervention received (e.g. number of text messages received, measures of use of allocated mobile application) and acceptability of intervention.

Search methods for identification of studies

Electronic searches

We identified trials through systematic searches of the following bibliographic databases on 7 January 2020:

- Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (Issue 1 of 12, 2020);
- Epub Ahead of Print, In-Process & Other Non-Indexed Citations, MEDLINE Daily and MEDLINE (Ovid, 1946 to 6 January 2020);
- Embase (Ovid, 1980 to 2020 week 1);
- CINAHL Plus (EBSCOhost, 1937 to 7 January 2020);
- Conference Proceedings Citation Index-Science (CPCI-S) on Web of Science (Clarivate Analytics, 1990 to 7 January 2020).

The search strategies are presented in Appendix 1. The Cochrane sensitivity-precision maximising RCT filter was applied to MEDLINE (Ovid) and adaptations of it to the other databases, except CENTRAL (Lefebvre 2011).

We carried out a search of www.ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) Search Portal (apps.who.int/trialsearch/) for ongoing or unpublished trials on 5 February 2020.

We imposed no restriction by date or language of publication.

We did not perform a separate search for adverse effects of mobile phone-based interventions targeting medication adherence. We considered adverse effects described in included studies only.

Due to the disruptions as a result of the Covid-19 pandemic, it was not possible to publish this review within 12 months of the search being conducted. We therefore repeated the search strategy on 8 January 2021, and screened these results, with potentially eligible studies added to 'Studies awaiting classification'.

Searching other resources

We checked the reference lists of all included studies and reviewed relevant articles for additional references. We also examined relevant retraction statements and errata for included studies.

Data collection and analysis

Selection of studies

Two review authors independently screened the titles and abstracts of all identified potential studies to decide whether to retrieve the full text (eligible or potentially eligible/unclear studies) or to discard the study. Two review authors independently screened the retrieved full texts to identify studies for inclusion and identify and record reasons for exclusion of the ineligible studies in the Characteristics of excluded studies table. We resolved any disagreements though discussion, and where necessary, a third review author arbitrated. We excluded any duplicates. We collated multiple reports of the same RCT into a single entry. We completed a PRISMA flow diagram (Liberati 2009).

Data extraction and management

We used a standardised, prepiloted form to extract data from the included studies for assessment of study quality and evidence synthesis. We contacted chief investigators for additional information where necessary. We extracted the following information.

- Methods: study design; total duration of study; study setting and date of study.
- Participants: number randomised; number lost to follow-up/withdrawn; number analysed; mean age; age range; gender; proportion meeting criteria of 'primary prevention'; and inclusion criteria and exclusion criteria.
- Interventions: intervention; comparison; concomitant medications; excluded medications; intervention delivery mechanism (text messages/MMS/mobile application/combined); how intervention was developed; if intervention was personalised; and frequency and duration of intervention receipt.
- Outcomes: primary and secondary outcomes specified and collected; adverse effects; and time points reported.
- Notes: funding for trial and notable conflicts of interest of trial authors.

Two review authors independently extracted data and resolved any differences by returning to the original study reports and discussion with a third review author where necessary. One review author transferred data into Review Manager 5 (Review Manager 2020). To ensure that there were no errors in data entry, another review author checked that the data entered into Review Manager 5 were consistent with those in the data extraction form.

Assessment of risk of bias in included studies

Two review authors independently assessed the risks of bias for each study using the criteria detailed in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). For each of the following domains, we graded the potential bias as high, low or unclear.

- Random sequence generation.
- Allocation concealment.
- Blinding of participants and personnel.
- Blinding of outcome assessment (objective and subjective self-reported outcomes assessed separately).
- Incomplete outcome data.
- Selective outcome reporting.
- Other biases (selective cluster recruitment for cluster RCTS).

We resolved disagreements by discussion. Where necessary, we consulted a third review author to arbitrate. We constructed a 'Risk of bias' table including justifications for our judgements. Where information relating to the risk of bias came from unpublished data or correspondence with an author, we noted this. We summarised the 'Risk of bias' judgements across different studies for each of the domains listed. When considering treatment effects, we accounted for the risk of bias for the studies that contributed to that outcome.

For other potential sources of bias, we assessed evidence for selective cluster recruitment for the included cluster RCTS. We assessed the blinding of outcome assessment domains separately for objectively-measured outcomes, and self-reported subjective outcomes. Given the nature of the interventions included in this review, it is likely that blinding of participants and personnel would be impossible, as would blinding of self-reported outcome assessment, so we expected trials to be categorised at high risk of bias for both of these domains. For the overall study assessment, we categorised a trial as being at low risk of bias if it was rated as low risk in all the domains listed above (with the exception of blinding of participants and personnel/self-reported outcome assessment). Trials that were at high or unclear risk of bias for any of the domains (except blinding of participants and personnel/self-reported outcome assessment) were categorised as being at high risk of bias.

Assessment of bias in conducting the systematic review

We conducted the review according to the published protocol and report any deviations from it in the Differences between protocol and review section (Palmer 2017).

Measures of treatment effect

We analysed dichotomous outcome data as odds ratios (ORs) with 95% confidence intervals (CIs). We analysed continuous outcome data as mean differences (MDs) with 95% CIs, or if a continuous outcome had been measured in multiple ways, as a standardised mean difference (SMD) with 95% CIs.

Unit of analysis issues

Due to the heterogeneity of the included studies' intervention content and delivery mechanisms, most of the results in the review are described narratively. However, in doing this we entered data in to RevMan to construct forest plots to aid data presentation without pooling. For cluster-randomised trials, we extracted the effect estimates adjusted for clustering where these were reported. Where cluster-randomised trials presented results which did not account for clustering, we recalculated effect estimates based on the 'effective sample size' derived from intracluster coefficients (ICCs) for CVD-related outcomes by Singh 2015 and Lee 2020 (specific ICCs used are noted in the footnotes of the corresponding data and analyses). For the two meta-analyses conducted in this review, one of the contributing trials had two eligible intervention arms (Bobrow 2016), and we therefore halved the number in the control group to avoid double-counting. We excluded intervention arms not appropriate for this review.

Dealing with missing data

We contacted investigators to obtain further information where necessary (e.g. when the study included a mixed population of participants who met the criteria for primary prevention and participants who met the criteria for secondary prevention, and when only a subset of participants had been prescribed CVD preventive medication). We also planned to contact investigators or study sponsors to obtain missing data (e.g. when a study was available as abstract only). We planned that where this was not possible, and the missing data were considered a potential source of serious bias, we would conduct a sensitivity analysis to explore the impact of including such studies in the overall assessment of results.

Assessment of heterogeneity

With the exception of two trials, both of which used a text messaging-based intervention to target blood pressure medication adherence and reported blood pressure outcomes (Bobrow 2016; Tobe 2019), we considered the included trials to be too methodologically heterogeneous to pool the data in a meta-analysis. We therefore describe most results narratively. We planned to use the I^2 statistic to measure heterogeneity across the trials for the analysis of each outcome. In constructing the narrative forest plots for those outcomes reported by multiple studies, we calculated the I^2 statistic and reported this. Had we considered the trials methodologically similar enough to pool, and had we identified moderate to substantial heterogeneity (an I^2 statistic between 30% and 100%), we would have reported it and examined possible causes according to our prespecified subgroup analyses, subject to having a sufficient number of studies.

Assessment of reporting biases

We planned that if the results from more than 10 trials could be pooled, we would use a funnel plot to explore possible small-study biases for the primary outcomes. However, we were able to pool only a maximum of two studies.

Data synthesis

We planned to carry out meta-analyses only if it was meaningful to do so (i.e. if the interventions, participants and outcome measures were similar enough for pooling to make sense). Two trials were considered similar enough to pool results (Bobrow 2016; Tobe 2019); this was on the basis that both studies evaluated interventions targeting blood pressure medication adherence using text messages only, and recorded blood pressure outcomes. We did not undertake meta-analyses for the rest of the included studies, as they were too heterogeneous in their content and delivery of their interventions. We present the effect estimates for outcomes reported by multiple studies in illustrative forest plots (without pooling); it should be noted that in transferring effect estimates from papers into Review Manager 5 using the generic inverse variance method, some CIs differed from those reported in the original paper by a decimal place, and where clustering has been accounted for using an external ICC (as described above), the CIs differ from those in the original report.

For the two studies pooled in meta-analyses, we used a fixed-effect model. In the presence of heterogeneity (an I^2 statistic in excess of 30%), we planned to examine whether this heterogeneity could be explained through our prespecified subgroup analyses. If these analyses accounted for the heterogeneity, we would only present the subgroup pooled effect estimates. If these subgroup analyses did not explain the heterogeneity, we would present results narratively. We intended to use fixed-effect meta-analysis and apply a conservative I^2 threshold to identify heterogeneity in this review to avoid overweighting smaller studies. This is because we consider that the heterogeneity observed in these behaviour-change trials will primarily be a result of differences in the content of the interventions and differences in risk of bias.

Subgroup analysis and investigation of heterogeneity

We had planned to conduct the following subgroup analyses for the primary outcome of adherence to treatment if there had been sufficient studies to pool in meta-analyses:

- income region (by World Bank income group) (World Bank 2017);
- how text messages were developed (i.e. theory-based, incorporating user views and based on evidence relating to factors influencing behaviour-targeted versus other);
- delivery mechanisms (i.e. mobile phone messaging only, mobile applications only, combined mobile phone messaging and application, combined application and other).

Due to the limited number of studies, we were unable to conduct subgroup analyses. Should more trials become available for future updates of this review, we will re-examine the planned subgroup analyses.

Sensitivity analysis

We planned to carry out a sensitivity analysis by only including studies with low risk of bias. As we only carried out a meta-analysis of two studies, we did not conduct a sensitivity analysis.

Summary of findings and assessment of the certainty of the evidence

We created a 'Summary of findings' table of narrative results for the following outcomes: objective measures of adherence to treatment (cholesterol and blood pressure), combined CVD events (fatal and non-fatal events), adverse events and cognitive outcomes. We used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence as it related to the studies that contributed data for each outcome. We used methods and recommendations described in Chapter 14 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2020) using GRADEpro software (GRADEpro GTD 2015). We justified decisions to downgrade the quality of studies using footnotes and made comments to aid readers' understanding of the review where necessary.

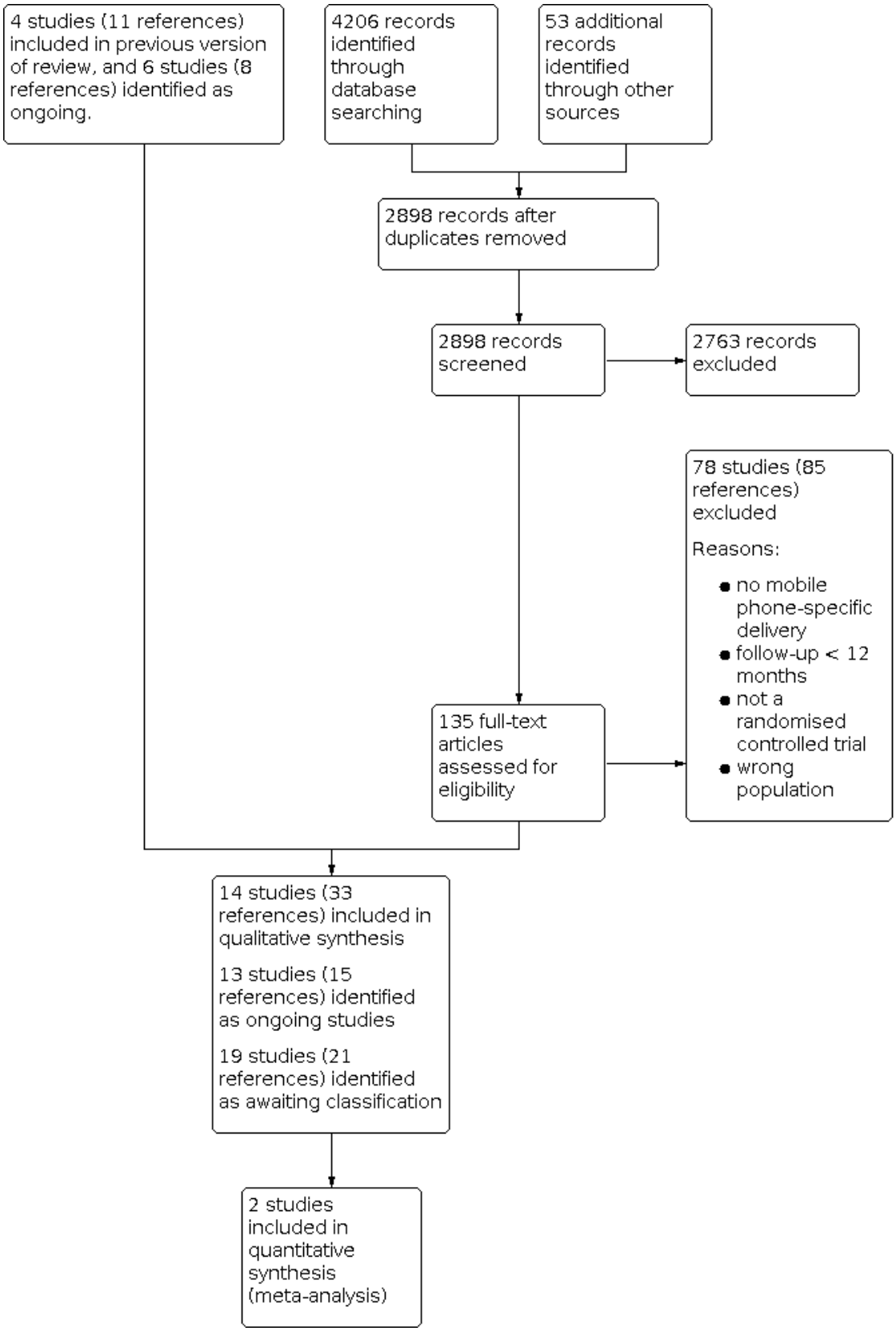
RESULTS

Description of studies

Results of the search

From the previous version of this review there were four included studies and six ongoing studies. The new search of the databases retrieved 4206 records, and the search of the clinical trial registers retrieved an additional 53 records. After de-duplication, we screened 2898 title and abstract records and excluded 2763 records. We assessed 135 full texts and excluded 85 references (78 studies). Combining the previous review and the updated search resulted in 13 ongoing studies (15 references), 19 studies (21 references) awaiting classification, and 14 studies (33 references) were eligible for inclusion. The flow diagram of search results is shown in Figure 1.

Figure 1. Study flow diagram.



Screening of the search that was repeated on 8 January 2021 resulted in a further 18 studies (19 references) awaiting classification.

Included studies

The Characteristics of included studies table presents details of the design, methods, participants, intervention, comparison and outcome measures for the studies included in this review. We identified 14 studies for inclusion, which were relatively heterogeneous, with particular variation in the nature (content and delivery) of the intervention, and the population.

Participants

The sample sizes of included studies ranged from 59 (Morillo-Verdugo 2018) to 9642 (Peiris 2019), with a total of 25,633 randomised participants across all 14 included studies.

Liu 2015 specified that participants must have had "no known cardiovascular disease" as an inclusion criterion, and therefore included 100% of participants meeting the criteria for primary prevention. Morillo-Verdugo 2018 was among participants living with HIV over 35 years of age, and "receiving active ART with at least 1 drug prescribed for the treatment of hypertension, dyslipidaemia, angina pectoris, cardiovascular prophylaxis, or type 2 diabetes"; 100% of participants met the criteria for primary prevention (personal communication with author).The other included studies had a mix of participants: in five studies, at least 90% of participants met the criteria of primary prevention (Choudhry 2018; Márquez Contreras 2019; McManus 2018; Párraga-Martínez 2017; Prabhakaran 2019); four studies included at least 78% primary-prevention participants (Bobrow 2016; He 2017; Logan 2012; Peiris 2019); and in one study approximately 65% of participants met the criteria for primary prevention, but results were reported separately for participants according to whether or not they had previously had a CVD event (Gulayin 2019). Saleh 2018 did not report the proportion of participants meeting the criteria for primary prevention, but stated that participants had to be registered at the primary healthcare centres "as diabetics or hypertensive and aged 40 years or more". We sought clarification from study authors on the proportion who had not had prior CVD events, but had not received this information at the time of submission. Tobe 2019 did not report the proportion of primary prevention participants (personal communication stated that this was not recorded), but inclusion criteria included age 18 years or more, uncontrolled hypertension (≥ 140/90 mmHg or ≥ 130/80 mmHg for diabetics), and stable on current dose of antihypertensive (if treated) for at least eight weeks.

There was heterogeneity between trials in the proportion of participants who were taking medication for the primary prevention of CVD. For four studies, having been prescribed medication for CVD prevention (anti-hypertensives or lipid-lowering medication) was an inclusion criterion, and therefore 100% of participants were receiving anti-hypertensive medication at baseline (Bobrow 2016; Choudhry 2018; Márquez Contreras 2019; McManus 2018). Logan 2012 included at least 89.1% of participants prescribed medication (hypertensive drugs or lipid-lowering drugs or aspirin, or a combination of these); almost 85% of participants in He 2017 were using antihypertensive medications at baseline; and Párraga-Martínez 2017 stated that 68.1% of their sample had been prescribed lipid-lowering medication (but did not mention other types of CVD prevention drugs). Based on communication with trial authors, at least 58% of participants in Prabhakaran 2019 were taking hypertensive or lipid-lowering medication. Almost half of participants in Peiris 2019 were taking at least one anti-hypertensive, lipid-lowering or anti-platelet medication. In Morillo-Verdugo 2018, 28% of participants were prescribed lipid-lowering medication, with additional prescriptions for other types of CVD drugs (data provided by drug class, so proportion of participants taking at least one CVD-related drug not available); and Tobe 2019 had 28% of participants on anti-hypertensive medications at baseline (personal communication). In Gulayin 2019, no participants were on CVD medication at baseline, with current statin use being an exclusion criterion, but the intervention sought to get participants on medication for hyperlipidaemia where indicated, and improve adherence to this medication. Liu 2015 did not report the proportion of participants prescribed medication, but explicitly stated that the intervention targeted adherence to medication among those on treatment. Similarly, Saleh 2018 did not report this proportion, but stated that the intervention targeted medication compliance.

The mean age of participants varied from approximately 49 years (Saleh 2018) to 67 years (McManus 2018). The proportion of women in the trial samples ranged from 9.4% (Morillo-Verdugo 2018) to 72% (Bobrow 2016).

Settings

All studies recruited from healthcare settings, whether from outpatients attending clinics or outreach/home visits co-ordinated by local health providers. Three studies were conducted in Spain: one recruited through four primary care centres in Huelva (Southern Spain) (Márquez Contreras 2019); one recruited participants living with HIV who had moderate or high cardiovascular risk from five tertiary hospitals (Morillo-Verdugo 2018); and one recruited participants from primary care clinics in three health districts of three Spanish autonomous communities (Párraga-Martínez 2017). Two trials were carried out in India: one recruited through community health centres in Haryana (North India) and Karnataka (South India) (Prabhakaran 2019), and one from primary health centres in Andhra Pradesh (South India) (Peiris 2019). Two trials recruited through primary healthcare centres in Argentina (Gulayin 2019; He 2017). Two studies were based in Canada: Logan 2012 recruited from the offices or clinics of physicians practising in metropolitan Toronto; and Tobe 2019 recruited through community healthcare provision from Canada's First Nations communities living on six reserves in Northern Ontario, Quebec and New Brunswick. Bobrow 2016 recruited from an outpatient chronic disease service in a single, large, public sector clinic in Cape Town, South Africa. Liu 2015 recruited from a health management centre in a hospital in Guangzhou, China. Choudhry 2018 recruited from primary care practice sites of a large multi-specialty group practice in Massachusetts, USA. McManus 2018 recruited from general practices in the UK. Finally, Saleh 2018 recruited from primary healthcare centres located in rural areas and Palestinian refugee camps across Lebanon.

Interventions

The content and delivery of the interventions varied across studies. In most of the trials, the interventions involved general health education, for example, targeting behaviours such as lifestyle modifications including healthy diet and physical activity, alongside messaging focusing on medication adherence for those

prescribed CVD medication (Gulayin 2019; He 2017; Liu 2015; Márquez Contreras 2019; Morillo-Verdugo 2018; Párraga-Martínez 2017; Prabhakaran 2019; Peiris 2019; Saleh 2018). The interventions evaluated by Bobrow 2016 and Choudhry 2018 were specifically designed to focus primarily on medication adherence, with only a few references to other lifestyle modifications such as diet and physical exercise. Similarly, Tobe 2019 focused on the importance of blood pressure control and the rationale for medical therapy to encourage adherence. Two trials examined interventions which primarily consisted of blood pressure telemonitoring; one included feedback (via their smartphone) and could review their readings (Logan 2012), and the other did not provide such feedback but relied on participants to send their readings via SMS (McManus 2018). These mobile telemonitoring interventions were considered to implicitly target adherence to treatment as well as other health behaviours important for the control of blood pressure.

Two studies delivered the intervention solely through educational and motivational mobile-phone text messages about hypertension and its medical therapy (Bobrow 2016; Tobe 2019), and one through a mobile application only, which allowed participants to record personal data, recommended BP levels as objectives, record the doctor's advice about the prescribed treatment, set reminder alarms, set a calendar of appointments or events, and record the results of the BP measurement (Márquez Contreras 2019). Three studies evaluated interventions involving text messages to participants, alongside additional components involving healthcare workers, such as a face-to-face counselling session (Liu 2015); pharmacotherapeutic follow-up and an individual motivational interview (led by pharmacists) to work towards the achievement of pharmacotherapeutic objectives (Morillo-Verdugo 2018), and additional training for healthcare providers focusing on clinical guidelines and provider-patient communication strategies (Saleh 2018). Two studies examined interventions involving training for healthcare providers in clinical guidelines, a mobile/tablet-based decision support system for clinical staff, and educational and motivational text messages directly to patients (Gulayin 2019; Prabhakaran 2019), and one study combined a tablet-based decision support system for clinical staff with interactive voice response messaging delivered to participants (Peiris 2019). Choudhry 2018 evaluated an intervention involving text message (as reminders and motivational support for adherence), pillboxes, mailed personalised progress reports, and an individually-tailored telephone consultation conducted by a staff clinical pharmacist. The intervention examined by He 2017 involved regular home visits from community health workers to providing education and counselling on lifestyle modification, home BP monitoring, and medication adherence skills; provision of an automatic home blood-pressure monitor and seven-day pill organiser; and individualised text messages to promote lifestyle changes and reinforce medication adherence. Párraga-Martínez 2017 involved a combination of text messages, written information, and self-completion cards for participants to record adherence to recommendations. Logan 2012 evaluated an intervention which involved the provision of a home blood-pressure monitoring device and feedback to participants' smartphones, alongside an automated fax providing detailed information on the participants' status to their physicians on the day before their next scheduled appointment. In McManus 2018, intervention participants were provided with a home blood-pressure monitoring device, and trained to send readings via a simple free SMS text-based telemonitoring service, which alerted participants to contact their healthcare providers in response to very high or very low readings or if their average blood pressure was above target, reminded them if insufficient readings were transmitted, and presented readings to clinicians via a web interface.

Most studies had a control group that received usual care (Choudhry 2018; He 2017; Liu 2015; Márquez Contreras 2019; Morillo-Verdugo 2018; Párraga-Martínez 2017; Peiris 2019; Saleh 2018). The control group in Logan 2012 received the same home blood-pressure monitoring equipment as the intervention group and a booklet containing information on the measurement of blood pressure, treatment of hypertension and goals of therapy. The control group in Bobrow 2016 received written information about hypertension and healthy living, and only received text messages that were sent to all trial participants, which primarily related to trial participation. The control group in Tobe 2019 received 'passive' text messages including healthy lifestyle and diet advice, with none of the content relating to blood pressure control. McManus 2018 had three arms: the telemonitoring arm (as described above), one arm which received usual care, and another group which was instructed to self-monitor blood pressure and at the end of each week record their readings on paper and send them to their healthcare provider. For the purposes of this review, we extracted data from the usual-care arm and excluded the self-monitoring arm. In Prabhakaran 2019, participants in the control group received 'enhanced' usual care, whereby training on clinical guidelines was provided to healthcare providers; charts on the management of conditions were displayed prominently at the outpatient clinics; and nurses provided a lifestyle advice pamphlet to each participant. Gulayin 2019 reported that the control group received usual care, but clinics were also provided with educational flyers and written material for display.

Outcomes

All studies reported at least one objective measure related to medication adherence. Thirteen studies measured blood pressure (Bobrow 2016; Choudhry 2018; He 2017; Liu 2015; Logan 2012; Márquez Contreras 2019; McManus 2018; Morillo-Verdugo 2018; Párraga-Martínez 2017; Prabhakaran 2019; Peiris 2019; Saleh 2018; Tobe 2019), and six studies measured cholesterol levels (at least one of the following: LDL-C, HDL-C, TC) (Choudhry 2018; Gulayin 2019; Liu 2015; Morillo-Verdugo 2018; Párraga-Martínez 2017; Prabhakaran 2019). Three studies provided outcome data relating to CVD events (McManus 2018; Peiris 2019; Tobe 2019) and one study reported on CVD-related deaths (Bobrow 2016).

Six studies explicitly reported adverse events, including adverse medication effects of statins, intervention-related adverse events and deaths (Bobrow 2016; He 2017; McManus 2018; Párraga-Martínez 2017; Prabhakaran 2019; Tobe 2019).

Nine studies reported indirect measures of adherence to treatment (our secondary outcomes). Three studies included outcome data on self-reported adherence measured using the Morisky-Green scale (for lipid-lowering medication (Gulayin 2019; Párraga-Martínez 2017) and for anti-hypertensive medication (He 2017)). Bobrow 2016 included self-reported adherence to medication measured using a visual analogue scale, in addition to a measure of 'proportion of days of medication covered' (defined as the proportion of participants with 80% or more days covered with blood pressure-lowering medication from prescribing and dispensing data routinely recorded in the clinical record,

pharmacy record and Chronic Dispensing Unit record). Choudhry 2018 reported medication adherence for hyperlipidaemia and hypertension, assessed using prescription claims data and measured as the mean proportion of days covered (PDC) over the 12 months after randomisation. Márquez Contreras 2019 reported the percentage of participants who took antihypertensive drugs correctly on 80% to 100% of days, measured using a Medication Event Monitoring System (MEMS). Prabhakaran 2019 recorded the proportion of participants who reported adherence to their anti-hypertensive drugs in the last seven days before the endline assessment. Morillo-Verdugo 2018 recorded the proportion of participants adherent to 'concomitant medication' measured with "the Morisky-Green questionnaire and pharmacy dispensing records". McManus 2018 recorded self-reported adherence using the 'Medication Adherence Rating Scale', but the study report lacks detail on how this was scored.

Three trials also included a measure of quality of life (measured with the EuroQol Group 5-Dimension Self-Report Questionnaire) (Bobrow 2016; McManus 2018; Peiris 2019).

Two trials reported on cognitive outcomes: Bobrow 2016 compared satisfaction with treatment between the trial arms, and Prabhakaran 2019 asked participants about their perceived quality of care.

Four trials reported data relating to our process measures, including satisfaction with the intervention (Párraga-Martínez 2017), adherence to the intervention home blood-pressure monitoring schedule (Logan 2012), proportion responding to messages (Bobrow 2016), and proportion opting to receive intervention text messages (Choudhry 2018).

Two trials reported on the costs associated with the intervention (He 2017; Prabhakaran 2019)

Further information requested

Of the trials which included participants who had or had not been prescribed CVD prevention medication, four studies did not report the proportion prescribed medication (Liu 2015; Prabhakaran 2019; Saleh 2018; Tobe 2019). We contacted authors for this information, and received it for two of the trials (Prabhakaran 2019; Tobe 2019). We also contacted authors of three trials (Bobrow 2016; Morillo-Verdugo 2018; Saleh 2018) for information relating to the proportion of participants who had previously experienced a CVD event and received this information for two trials (Bobrow 2016; Morillo-Verdugo 2018).

Excluded studies

See Characteristics of excluded studies table for details of excluded studies which narrowly missed the inclusion criteria.

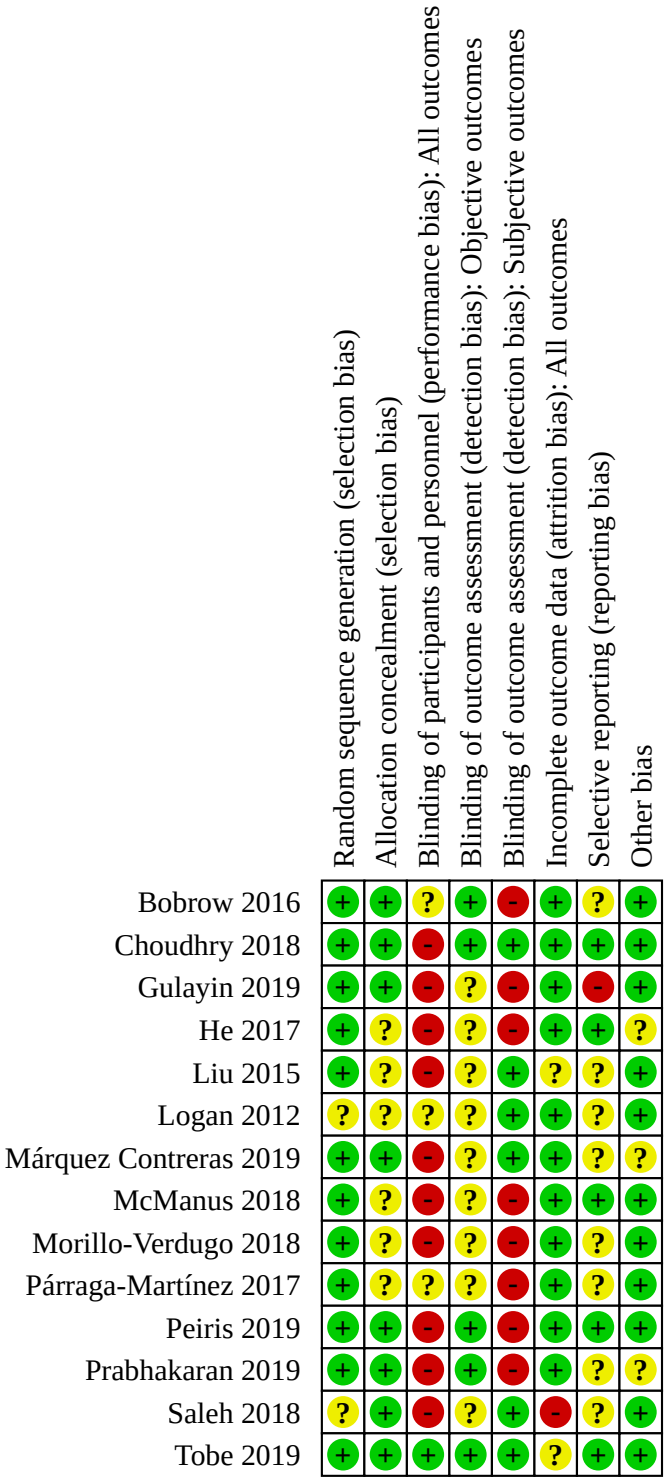
Ongoing studies

We identified 13 ongoing studies (see Characteristics of ongoing studies table).

Risk of bias in included studies

Details of the risk of bias assessments for each of the included studies are presented in the 'Risk of bias' tables in the Characteristics of included studies table, and in Figure 2

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Twelve studies reported adequate random sequence generation and were at low risk of bias for this domain (Bobrow 2016; Choudhry 2018; Gulayin 2019; He 2017; Liu 2015; Márquez Contreras 2019; McManus 2018; Morillo-Verdugo 2018; Párraga-Martínez 2017; Peiris 2019; Prabhakaran 2019; Tobe 2019). Two studies did not provide sufficient information and were therefore at unclear risk of bias for random sequence generation (Logan 2012; Saleh 2018).

Eight studies described their allocation concealment adequately and were at low risk of bias in this domain (Bobrow 2016; Choudhry 2018; Gulayin 2019; Márquez Contreras 2019; Peiris 2019; Prabhakaran 2019; Saleh 2018; Tobe 2019). The other six studies did not provide sufficient information on their allocation procedures and were therefore at unclear risk of bias for allocation concealment (He 2017; Liu 2015; Logan 2012; McManus 2018; Morillo-Verdugo 2018; Párraga-Martínez 2017).

Blinding

In all but one of the included studies, the nature of the interventions precluded blinding of participants, the exception being Tobe 2019 which compared 'active' messages with 'passive messages' including general health information, meaning it would not be obvious to participants whether they were in the intervention or control group. This study also blinded personnel, so was at low risk of bias in this domain. In 10 studies, personnel were not blinded to group assignment (Choudhry 2018; Gulayin 2019; He 2017; Liu 2015; Márquez Contreras 2019; McManus 2018; Morillo-Verdugo 2018; Peiris 2019; Prabhakaran 2019; Saleh 2018) and were at high risk of bias this domain. The remaining three studies were at unclear risk of bias: two of them stated that personnel were blinded (Bobrow 2016; Párraga-Martínez 2017), and one study was not clear whether personnel were blinded (Logan 2012).

For the blinding of objective outcome assessment domain, five studies provided sufficient detail relating to the blinding of outcome assessors and were at low risk of bias for this domain (Bobrow 2016; Choudhry 2018; Peiris 2019; Prabhakaran 2019; Tobe 2019). Nine studies did not provide adequate detail relating to whether or not outcome assessors were blinded, the nature of data collection, or the nature of data entry, or both, and so were judged as being at unclear risk of bias in this domain (Gulayin 2019; He 2017; Liu 2015; Logan 2012; Márquez Contreras 2019; McManus 2018; Morillo-Verdugo 2018; Párraga-Martínez 2017; Saleh 2018).

Eight of the included studies reported self-reported subjective outcomes for extraction. All were judged to be at high risk of bias for this domain, as the participants could not be blinded to their allocation, and therefore this may have resulted in biased self-reported outcomes (Bobrow 2016; Gulayin 2019; He 2017; McManus 2018; Morillo-Verdugo 2018; Párraga-Martínez 2017; Peiris 2019; Prabhakaran 2019). This domain did not apply to the six other studies, as they did not report subjective outcomes. We assessed these as low risk of bias to provide a complete risk of bias assessment (Choudhry 2018; Liu 2015; Logan 2012; Márquez Contreras 2019; Saleh 2018; Tobe 2019).

Incomplete outcome data

Most of the included studies had high rates of follow-up (85% or greater) with no evidence of differential loss to follow-up, and reported sensitivity analyses finding consistent results or used appropriate methods to impute missing data; we therefore judged them to be at low risk of bias for the incomplete outcome data domain (Bobrow 2016; Choudhry 2018; Gulayin 2019; He 2017; Logan 2012; Márquez Contreras 2019; McManus 2018; Morillo-Verdugo 2018; Párraga-Martínez 2017; Peiris 2019; Prabhakaran 2019).

One study reported that 27.5% of participants did not attend for follow-up, and that they differed from those who did attend for follow-up based on several characteristics. The study also reported that these missing values were likely to have little impact on the primary outcome, based on sensitivity analyses. However, it is unclear whether this may have affected other outcomes, and so we rated this study at unclear risk of bias for this domain (Liu 2015). We judged a second study to be at unclear risk of bias for this domain, as 14% loss to follow-up was reported, but no further information nor analyses relating to these participants were provided (Tobe 2019).

Finally, Saleh 2018 was considered to be at high risk of bias for incomplete outcome data, as 28% of participants in the intervention group had no outcome data compared to only 1% in the control group, and this discrepancy was not explained.

Selective reporting

Five studies were at low risk of bias for selective reporting on the basis that they reported all (or at least main) outcomes as specified in their published protocols, and the trials were registered prior to start of recruitment (Choudhry 2018; He 2017; McManus 2018; Peiris 2019; Tobe 2019). Gulayin 2019 was considered to be at high risk of bias for this domain as the "proportion of patients with moderate and high CVD risk who have reduced their LDL-c by 30% and 50% respectively" was specified as an outcome in the protocol, but no results for this are reported.

The rest of the studies were at unclear risk of bias for selective reporting. Bobrow 2016 reported outcomes as planned in their protocol, with the exception of one outcome that was flagged in protocol, but not in the trial report ('hypertension knowledge'). This trial began recruiting in June 2012, but details of the protocol were not registered until December 2013, and so we cannot be certain as to what was planned before the trial began. Three trials also appeared to have been registered after recruitment had begun, with no published protocol identified (Liu 2015; Logan 2012; Saleh 2018). We could find no protocol for Márquez Contreras 2019, and while the report stated the trial had been registered it was unclear whether this was prior to recruitment. We found no protocol nor trial registry entry for Morillo-Verdugo 2018. Párraga-Martínez 2017 reported all outcomes as planned in the protocol, with the exception of cardiovascular events occurring during the study period. This was considered an important outcome, but it was not clear whether this outcome was not reported because no events occurred. In Prabhakaran 2019 not all of the secondary outcomes (health-related quality of life and costs) were reported, but authors stated that the cost-effectiveness analysis would be conducted if the intervention showed a substantial effect, which it did not. The supplementary materials for this trial listed the adverse events to be recorded, but no mention of adverse events is made in the trial report, although it is not clear whether this is because none occurred.

Other potential sources of bias

For other potential sources of bias, we assessed evidence for selective cluster recruitment for the included cluster-RCTS. Four studies were considered at low risk of bias for this domain, with little difference between arms in relevant baseline characteristics (Choudhry 2018; Gulayin 2019; Peiris 2019; Saleh 2018). Three studies were at unclear risk of bias, either due to some imbalances in baseline characteristics (but it was not clear whether these would affect conclusions drawn) (He 2017; Prabhakaran 2019) or because key baseline characteristics were not measured (Márquez Contreras 2019). The remaining trials were not parallel RCTs and so this domain was not applicable; we judged them to be at low risk, to provide a complete 'Risk of bias' assessment (Bobrow 2016; Liu 2015; Logan 2012; McManus 2018; Morillo-Verdugo 2018; Párraga-Martínez 2017; Tobe 2019).

Effects of interventions

See: **Summary of findings 1** Mobile phone interventions compared to usual care for improving adherence to medication prescribed for primary prevention of cardiovascular disease

We did not pool results in a meta-analysis for most of the trials, as we deemed the content and delivery mechanisms of the interventions, and the study populations, too heterogeneous to allow meaningful pooling. The exceptions to this were the Bobrow 2016 and Tobe 2019 trials, both of which delivered the intervention solely through text messages about hypertension and it's medical therapy to target adherence, and recorded blood pressure outcomes (systolic blood pressure, and 'controlled' blood pressure).

In generating the illustrative forest plots, we also checked heterogeneity statistically (I^2 greater than 85% for systolic blood pressure (SBP) and for diastolic blood pressure (DBP); I^2 = 55% for controlled blood pressure; I^2 = 39% for total cholesterol; I^2 = 24% for LDL-C; I^2 = 0% for HDL-C). Based on these findings, we gave further consideration to pooling results from the three studies which reported HDL-C (Liu 2015; Morillo-Verdugo 2018; Párraga-Martínez 2017) and from the five studies which reported LDL-C (Choudhry 2018; Gulayin 2019; Liu 2015; Morillo-Verdugo 2018; Párraga-Martínez 2017). However, we still considered the interventions too diverse to warrant meaningful pooling: specifically, one intervention included face-to-face counselling alongside text-messaging (Liu 2015); one consisted of written information and text messages (Párraga-Martínez 2017); one involved pharmacotherapeutic follow-up and an individual motivational interview (led by pharmacists), in addition to text messages (Morillo-Verdugo 2018); another involved training for healthcare providers in clinical guidelines, a mobile/tablet-based decision support system for clinical staff, and educational and motivational text messages directly to patients (Gulayin 2019); and Choudhry 2018 evaluated an intervention involving text messages (as reminders and motivational support for adherence), pillboxes, mailed personalised progress reports, and an individually-tailored telephone consultation conducted by a staff clinical pharmacist.

We present results narratively below, and in Analysis 1.1; Analysis 1.2; Analysis 1.3; Analysis 1.4; Analysis 1.6; Analysis 1.7.

Primary outcomes

Objective measures of adherence to treatment

Cholesterol

Five trials reported LDL-C levels (Analysis 1.1), two of which showed reductions in LDL-C with confidence intervals excluding no effect: MD −9.20 mg/dL, 95% CI −17.7 to −0.70 (Párraga-Martínez 2017) and MD −5.30 mg/dL, 95% CI −8.30 to −2.30 (Choudhry 2018).

Two trials reported results consistent with no intervention effect on LDL-C: MD −1.60 mg/dL, 95% CI −25.78 to 22.58 (Morillo-Verdugo 2018) and MD 0.77 mg/dL, 95% CI −4.64 to 6.18 (Liu 2015) (note: we converted mmol/L cholesterol to mg/dL using a multiplier of 38.67, as recommended by Rugge 2011).

Gulayin 2019 reported results separately according to the baseline CVD risk of participants as follows: moderate CVD-risk participants MD −3.60 mg/dL, 95% CI −13.5 to 6.03, and high CVD risk-participants MD −7.70 mg/dL, 95% CI −25.8 to 10.40. Morillo-Verdugo 2018 also reported the proportion of participants with 'controlled' LDL-C (without specifying the cut-off applied), with no appreciable difference between the intervention arm (64.3%) and the control arm (63.2%).

We judged the evidence relating to the intervention effect on LDL-C to be of low certainty, due to all but one of the trials contributing to this comparison being at unclear risk of bias across multiple domains, and the inconsistency in effect estimates across studies (Summary of findings 1).

Of the four trials recording total cholesterol (Analysis 1.2), two found evidence of intervention benefit: MD −10.05 mg/dL, 95% CI −17.01 to −3.09 (Liu 2015) and MD −9.70 mg/dL, 95% CI −19.10 to −0.30 (Párraga-Martínez 2017).

The other two reported results consistent with no intervention effect: MD −4.70 mg/dL, 95% CI −26.45 to 17.05 (Morillo-Verdugo 2018) and MD −1.80 mg/dL, 95% CI −6.30 to 2.70 (Prabhakaran 2019). Morillo-Verdugo 2018 also reported the proportion of participants with 'controlled' total cholesterol as follows: intervention arm 64.3% and the control arm 62.5%.

None of the three trials found evidence for an adverse effect on HDL-C (Analysis 1.3): MD 1.16 mg/dL, 95% CI −1.55 to 3.87 (Liu 2015); MD 0.10 mg/dL, 95% CI −2.60 to 2.80 (Párraga-Martínez 2017); MD 1.50, 95% CI −6.11 to 9.11 (Morillo-Verdugo 2018).

Blood pressure

Thirteen studies reported at least one blood pressure outcome. Overall, we judged the evidence about blood pressure to be of low certainty, due to substantial inconsistency between studies in the degree to which the outcomes were affected, and because most of the trials were at unclear risk of bias across multiple domains (Summary of findings 1).

Of the 13 studies recording systolic blood pressure, nine showed a reduction in the intervention arm compared to the control (Analysis 1.4). For four of these studies, the reduction in systolic blood pressure had confidence intervals which excluded no effect, as follows: MD −6.60 mmHg, 95% CI −8.60 to −4.60 (He 2017); MD −12.45 mmHg, 95% CI −15.02 to −9.88 (Liu 2015); MD −7.10 mmHg, 95% CI −11.61 to −2.59 (Logan 2012); MD −4.70 mmHg, 95% CI −7.00 to -2.40 (McManus 2018).

For the eight studies in which the confidence interval included no effect, the mean difference ranged from −3.96 mmHg (Morillo-Verdugo 2018) to 0.83 mmHg (Párraga-Martínez 2017). Choudhry 2018 recorded an increase in systolic blood pressure in the intervention arm of 2.80 mmHg with a confidence interval excluding no effect: 95% CI 0.30 to 5.30. The meta-analysis (Analysis 1.5) of the two trials which evaluated an intervention targeting adherence to blood pressure medication delivered solely by SMS messaging provided a pooled MD of −1.55 mmHg, 95% CI: −3.36 to 0.25, I^2 = 0% (Bobrow 2016; Tobe 2019).

Eleven trials recorded diastolic blood pressure (Analysis 1.6). Four found a reduction in the intervention arm with confidence intervals excluding no effect: MD −5.40 mmHg, 95% CI −6.80 to −4.00 (He 2017); MD −12.23 mmHg, 95% CI −14.03 to −10.43 (Liu 2015); MD −3.90 mmHg, 95% CI −6.45 to −1.35 (Logan 2012); MD −1.30 mmHg, 95% CI −2.50 to −0.10 (McManus 2018). The remaining seven trials reported mean differences in diastolic blood pressure ranging from −3.64 mmHg, 95% CI −9.03 to 1.75 (Márquez Contreras 2019) to 1.64 mmHg, 95% CI −0.55 to 3.83 (Párraga-Martínez 2017).

Seven studies reported 'controlled' blood pressure as an outcome (Analysis 1.7). Estimates varied from negligible effects (OR 1.01, 95% CI 0.76 to 1.34) (Peiris 2019) to large improvements in blood pressure control (OR: 2.41, 95% CI 1.57 to 3.68) (He 2017), athough for all but one study (He 2017), confidence intervals encompassed no effect. The pooled analysis (Analysis 1.8) of two trials which evaluated an intervention targeting adherence to blood pressure medication delivered solely by SMS messaging indicated a modest beneficial intervention effect: OR 1.32, 95% CI 1.06 to 1.65, I^2 = 0% (Bobrow 2016; Tobe 2019).

Heart rate

No studies reported heart rate.

Urinary 11-dehydrothromboxane B2

No studies reported urinary 11-dehydrothromboxane B.

Combined cardiovascular disease event (fatal or non-fatal events)

One trial reported on deaths due to CVD (Bobrow 2016), and three trials recorded non-fatal CVD events (McManus 2018; Peiris 2019; Tobe 2019). For three studies the effect estimate was in the direction of harm (Bobrow 2016; McManus 2018; Peiris 2019), and for the fourth it was in the direction of intervention benefit (Tobe 2019). However, the number of events in each trial was low and all effect estimates had wide 95% confidence intervals, encompassing no effect (Analysis 1.9). For further detail see 'fatal CVD events' and 'non-fatal CVD events' in Secondary outcomes.

Adverse effects

Based on six trials, we found moderate-certainty evidence that the mobile phone-based interventions under study did not lead to adverse events (Summary of findings 1). The evidence was of moderate certainty, due to the studies being at unclear risk of bias across multiple domains. Bobrow 2016 (1372 participants) reported no adverse events attributable to the intervention. Párraga-Martínez 2017 (304 participants) reported that there were no differences between groups in experiencing adverse effects of statins (intervention group: 7 events; control group: 10 events), and no participants reported intervention-related adverse events. McManus 2018 reported that potential side-effects were similar between the groups. He 2017 stated that no adverse events were reported. Prabhakaran 2019 provided a list of adverse events that would be recorded, although they are not reported on in the trial report, and it is unclear whether this is because none occurred. However, Prabhakaran 2019 did report the number of deaths by arm (34 deaths in the intervention group and 21 deaths in the control group), but not the causes of death. Tobe 2019 stated that there were no reports of hypotension, and there were two deaths in the intervention arm: one due to pre-existing cancer and one in a car accident (as a passenger). The other trials did not report on adverse events (Choudhry 2018; Gulayin 2019; Liu 2015; Logan 2012; Márquez Contreras 2019; Morillo-Verdugo 2018; Peiris 2019; Saleh 2018).

Secondary outcomes

Indirect measures of adherence to treatment

Included studies reported a variety of different measures relating to adherence to prescribed medication. An overview of the trial results for indirect measures of medication adherence is presented in Table 1.

Six studies reported on adherence to blood pressure-lowering medication, of which five found evidence of intervention benefit. Bobrow 2016 (1372 participants) presented 12-month outcome data for the median difference in the proportion of days covered by dispensed blood pressure medication, finding evidence for a modest benefit for both the information-only text-messaging intervention group (83.3% with intervention versus 79.2% with control; median difference 5.2, quartiles 1 - 3: 1.5 to 8.9; P = 0.006), and the interactive text-messaging group (83.3% with intervention versus 79.2% with control; median difference: 3.8, quartiles 1 - 3: 0.03 to 7.6; P = 0.048), compared with the control group receiving usual care. There were similar results for the outcome of achieving 80% or more days covered (information-only text-messaging group versus control: OR 1.86, 95% CI 1.39 to 2.49; P < 0.001; interactive text-messaging group versus control: OR 1.60, 95% CI 1.20 to 2.16; P = 0.002) (it is not clear how the underlying proportions compared, as the authors did not report the proportion achieving 80% or more days covered for the control group). However, there was no evidence of benefit for the outcome of self-reported medication adherence (information-only text-messaging group versus control: median difference 0.04, quartiles 1 - 3: −0.1 to 0.2; P = 0.70; interactive text-messaging group versus control: median difference 0.02, quartiles 1 - 3: −0.2 to 0.2, P = 0.80). He 2017 found evidence of intervention benefit, with 66.1% of the intervention group reporting high medication adherence (based on the Morisky-Green test) compared with 53.0% of the control group at 1 year (P < 0.001). Similarly, Prabhakaran 2019 reported higher medication adherence at 1-year follow-up in the intervention group (81.1%) compared to the control group (57.9%) (P < 0.001) (based on the proportion who reported taking their drugs on all seven days prior to endline assessment). Márquez Contreras 2019 reported a greater proportion of participants in the intervention group taking their blood-pressure medication correctly on 80% to 100% of days recorded via MEMS (86.3% versus 62.7%, P = 0.064). Based on the mean proportion of days covered over 12 months as indicated by prescription data, Choudhry 2018 reported modest beneficial intervention effect (MD 8.5, 95% CI 5.4 to 11.7). No evidence of intervention benefit was reported by McManus 2018, based on a mean self-reported adherence score (MD 0.02, 95% CI −0.20 to 0.25).

Three studies recorded adherence to lipid-lowering medication. Choudhry 2018 recorded the mean proportion of days covered for lipid-lowering medication based on prescription data, with a slightly higher level of adherence evident in the intervention group (MD 4.5, 95% CI 2.1 to 6.8). Párraga-Martínez 2017 found evidence of intervention benefit for the proportion of participants reporting adherence to lipid-lowering therapy (measured using the Morisky-Green test) at two years post-randomisation (77.2% with intervention versus 64.1% with control; P = 0.029), whereas no beneficial effect was recorded for self-reported adherence to lipid-lowering therapy (again measured using the Morisky-Green test) in Gulayin 2019 (moderate CVD-risk participants: intervention 46.9%, control 50.1%, P = 0.799; high CVD-risk participants: intervention 30.3%, control 45.8%, P = 0.262).

Finally, Morillo-Verdugo 2018 reported adherence to 'concomitant medication' (which could have referred to various CVD-related medication types - see Characteristics of included studies for more detail), with higher adherence recorded in the intervention group (87.7%) compared with the control group (58.3%).

Fatal cardiovascular events

Bobrow 2016 (1372 participants) reported that two participants in the information-only text-messaging group died due to ischaemic heart disease, two participants in the interactive text-messaging group died due to congestive cardiac failure, and there were no deaths in the control group known to be due to CVD. There were slightly more participants in the usual-care arm who were lost to follow-up due to 'lost contact' (14 participants), compared to the information SMS arm (seven participants), and the interactive SMS arm (seven participants). It is therefore possible that this differential lost to follow-up due to lost contact could have underestimated deaths, including those due to CVD, in the usual-care arm.

Non-fatal cardiovascular events

McManus 2018 reported that cardiovascular events (new atrial fibrillation, angina, myocardial infarction, coronary artery bypass graft or angioplasty, stroke, peripheral vascular disease, or heart failure) were recorded in nine participants in the control group, and 11 in the intervention group. Tobe 2019 stated that one participant in the control group had a stroke, and one participant in the intervention group had a myocardial infarction. Peiris 2019 reported that 107/4348 participants in the intervention group reported a new CVD event, compared with 62/4294 in the control group, but the confidence interval was wide and encompassed benefit and harm (OR 1.42, 95% CI 0.78 to 2.62).

Health-related quality of life assessed using validated instruments

Bobrow 2016 reported the median difference in quality of life as measured by the Euro-Qol 5-Dimension Index, finding no effect of the information-only text messages (median difference 0.01, quartiles 1 - 3: −0.01 to 0.02; P = 0.50) or the interactive text messages (median difference: 0.003, quartiles 1 - 3: −0.02 to 0.02; P = 0.73) compared with the control group. McManus 2018 and Peiris 2019 also reported on quality of life with a mean difference of −0.03, 95% CI −0.06 to −0.001; P = 0.0384, and 0.02, 95% CI 0.00 to 0.04, P = 0.03, respectively.

Cognitive outcomes

Bobrow 2016 measured satisfaction with treatment and found no evidence of difference between intervention arms and control arm (information-only text-messaging group versus control: median difference 0, quartiles 1 - 3: −0.3 to 0.3; P > 0.99; interactive text-messaging group versus control: median difference 0, quartiles 1 - 3: −0.3 to 0.3; P > 0.99). Prabhakaran 2019 reported on perceived quality of care, with little difference observed between the two groups (intervention: 96.6%, control: 95.0%).

Costs

Two studies provided information on costs. He 2017 reported the total cost per participant (intervention and healthcare costs) as follows: mean costs intervention arm: USD 178.6, control arm: USD 67.6 (MD USD 102.7, 95% CI 61.0 to 144.4). In relation to costs, Choudhry 2018 stated "clinical pharmacists spent a total of 985 hours conducting these calls, or 29 minutes per patient. Assuming a mean annual pharmacist salary of USD 120 000, this amounts to USD 30 per patient per year. Our intervention also had other components although their marginal costs were small".

Process measures

Four studies reported relevant process measures. Párraga-Martínez 2017 recorded satisfaction with the intervention, finding that 90.8% (95% CI 85.9 to 95.7) of the 155 intervention-group participants reported being satisfied or very satisfied with the intervention at two years' post-randomisation. Logan 2012 recorded a 65.4% (standard deviation 30) adherence rate to the home blood-pressure measurement schedule (taking a minimum of eight readings per week) in the intervention group. Bobrow 2016 reported that 50% of participants allocated to the interactive SMS intervention arm responded to messaging. Choudhry 2018 reported that of the 1069 intervention participants who received a telephone consultation, 194 (18.1%) opted in to receive text messages, and among all 2038 intervention participants, 1804 (88.5%) were sent quarterly progress reports.

DISCUSSION

Summary of main results

This review provides low-certainty evidence about the effects of adherence interventions delivered by mobile phone, with some trials reporting modest benefits and other no benefits. There was moderate-certainty evidence that the interventions did not cause harm. In our review, we identified 14 trials, of which two were at low risk of bias (Choudhry 2018; Peiris 2019). The trials varied widely in the behaviours targeted, content and delivery mechanisms of the interventions, and the populations targeted. Due to these differences, we mostly summarised results narratively.

The evidence for the intervention effect on LDL cholesterol was of low certainty. Two of the five studies reporting LDL cholesterol as an outcome recorded evidence of intervention benefit, albeit of a modest size (Choudhry 2018; Párraga-Martínez 2017).

The body of evidence relating to the effect of mobile phone-based interventions on blood pressure was also of low certainty. Four of the 13 studies recording systolic blood pressure showed evidence of intervention benefit, with confidence intervals excluding no effect (He 2017; Liu 2015; Logan 2012; McManus 2018). The same four trials also demonstrated a reduction in diastolic

blood pressure associated with the intervention (He 2017; Liu 2015; Logan 2012; McManus 2018). The direction of the point estimates was more consistently positive for the outcome of 'controlled' blood pressure, although the confidence intervals excluded no effect in only one trial (He 2017). Pooled analysis of two trials showed there was little or no benefit for systolic blood pressure for interventions delivered solely through educational and motivational text messages about hypertension and its medical therapy, although there was a modest increase in the proportion of participants with 'controlled' blood pressure (Bobrow 2016; Tobe 2019).

Nine studies reported indirect measures of medication adherence, of which seven reported evidence of intervention benefit (Bobrow 2016; Choudhry 2018; He 2017; Márquez Contreras 2019; Morillo-Verdugo 2018; Párraga-Martínez 2017; Prabhakaran 2019), ranging from a relatively small increase in adherence in the intervention arm based on prescription data (Bobrow 2016; Choudhry 2018) to the largest effect estimates (a 23.1% and a 27.9% absolute increase in adherence) recorded through self-reported data (Morillo-Verdugo 2018; Prabhakaran 2019).

Based on four studies, there was very low-certainty evidence relating to the intervention effect on combined (fatal and non-fatal) CVD events (Bobrow 2016; McManus 2018; Peiris 2019; Tobe 2019).

Overall completeness and applicability of evidence

The studies were conducted in a range of high, upper-middle, and lower-middle settings and some specifically targeted more disadvantaged settings within those countries, providing reasonable confidence in the applicability of results across settings. Given that one of our inclusion criteria was that trials have a minimum of one-year follow-up, we can be confident that our results are applicable to longer-term, sustained medication adherence behaviours and outcomes. Few studies reported on fatal or non-fatal cardiovascular events, meaning we were unable to establish whether the modest benefits observed in individual trials for cholesterol and blood pressure translated into such patient-relevant outcomes. In the trials involving clinical decision support systems, whereby prescriptions and dosages may have been altered during the study period, we cannot be sure of the contribution of increased medication adherence to the reductions in cholesterol and blood pressure reported. The relative contribution of improved medication adherence is also uncertain in the trials which included a mix of participants who had and had not been prescribed CVD medication, and those which targeted lifestyle modifications alongside medication-taking behaviour. Furthermore, in many of these trials, adherence to medication was a secondary rather than a primary outcome, meaning that these studies were not designed around the focus of this review.

Quality of the evidence

Using GRADE methodology, we assessed the certainty of the evidence for our narrative synthesis of objective outcomes of medication adherence (LDL-C, SBP and DBP), cognitive outcomes and adverse events. The evidence was of low certainty across all outcomes, with the exception of adverse events, for which we rated the evidence as of moderate certainty. We downgraded the certainty of the evidence for objective outcomes of medication adherence by one level as a result of inconsistency in effect estimates which spanned both clinically-meaningful improvements and null effects. We downgraded the certainty of the evidence for all five outcomes considered by one level because most of the included studies were at high risk of bias. Eleven of the studies were at unclear risk of bias for at least two of the domains, indicating inadequate reporting of the trial methods in these studies, which limited our ability to make clear judgements about the level of risk of bias. Finally, the evidence relating to the cognitive outcomes of satisfaction with treatment and perceived quality of care was also downgraded for indirectness, because this was based on two trials measuring different outcomes. Half of the trials in this review randomised by clusters rather than individuals, and not all measured indicators of adherence at baseline, so there was uncertainty about the extent of imbalanced relevant baseline characteristics in these trials.

Potential biases in the review process

Our inability to conduct a meta-analysis for most outcomes means that this review cannot benefit from examining pooled effect estimates based on larger sample sizes than the individual trials. Furthermore, publication bias, whereby trials with positive findings are more likely to be published, may have biased the selection of included studies for this review. However, we tried to overcome this through searching clinical trial registries for prospectively-registered trials. We decided to only include trials with a minimum of one-year follow-up in order that results were applicable to longer-term sustained behaviour change in adherence, which would therefore be more important in improving health status. This means that we are unable to comment on the effectiveness of mobile phone-based interventions for short-term adherence to medication prescribed for the primary prevention of CVD.

Agreements and disagreements with other studies or reviews

Our findings of mixed evidence for the effects of mobile phone-delivered interventions to increase adherence to medication prescribed for the primary prevention of CVD and no reported harms are consistent with those of a Cochrane Review examining the effectiveness of text-messaging interventions to improve adherence to medication prescribed for the secondary prevention of CVD (Adler 2017). These findings are broadly consistent with systematic reviews of mhealth interventions to improve medication adherence across conditions, although these reviews included short-term studies and non-RCT designs, which are subject to bias (Anglada-Martinez 2015; Park 2014b; Ng 2020). One systematic review examining RCTs of monitoring and messaging interventions targeting medication adherence for the management of type 2 diabetes found no evidence for an improvement in medication adherence in their pooled meta-analyses of five trials (Farmer 2016). Our finding that pooled analyses of interventions delivered by text messaging alone indicated small benefits, some of which achieved statistical significance, is consistent with the findings from trials using SMS alone targeting adherence to HIV medication, which also report small benefits of borderline clinical and statistical significance (Da Costa 2012; Orrell 2015; Pop-Eleches 2011; Sabin 2015). The three (out of four) studies reporting evidence of intervention benefit for lowering blood pressure with confidence intervals excluding no effect were the only studies which included the provision of home blood-pressure monitoring systems in combination with mobile phones in the intervention. These positive intervention effects are consistent with the modest benefits of monitoring interventions in general

(Carrasco 2008; Lim 2011; McKinstry 2013; Yoo 2009). The small or modest benefits reported may reflect the challenges involved in improving adherence, and overall inconclusive findings relating to adherence interventions in general, which have previously been noted in a Cochrane Review of all adherence interventions (Nieuwlaat 2014).

AUTHORS' CONCLUSIONS

Implications for practice

Our results are based on 14 trials, of which two were considered to be at low risk of bias.

One trial at low risk of bias reported a reduction in low-density lipoprotein cholesterol (LDL-C) of 5.3 mg/dl (Choudhry 2018). The Cholesterol Treatment Trialists' Collaboration estimates that for each 1 mmol/L (38.67 mg/dL) reduction in LDL-C there is a consistent 20% relative risk reduction for major vascular events, regardless of baseline risk (CTT 2012). So this equates to a 2.7 % relative risk reduction in major cardiovascular events. The other four trials measuring LDL-C as an outcome reported intervention effects ranging from a 9.2 mg/dL reduction to a 0.77 mg/dL increase, meaning that even the larger of these effects would have a small or modest impact on clinical outcomes.

No trials at low risk of bias reported reductions in blood pressure (BP). All three of the trials of interventions involving a home blood-pressure monitoring system alongside telemedicine support via mobile phone reported reductions in systolic BP of −6.6, −7.1,and 4.7 mmHg respectively, and of diastolic BP of −5.4, −3.9 and −1.3 respectively (He 2017; Logan 2012; McManus 2018). Differences in the effects may be due to differences in the control group (standard care or self-monitoring without mobile phone-based telemedicine support), differences in the content and media for delivering the telemedicine support, chance or bias. A 10 mg drop in systolic BP or a 5 mg drop in diastolic BP gives 22% fewer coronary events at one year and 41% fewer strokes, so these effects are clinically important (Collins 1990; Law 2009). Those considering implementing similar interventions should take into account the risks of bias in these trials and whether additional costs are incurred. Liu 2015 also reported clinically important reductions in systolic and diastolic BP of −12 mmHg associated with an intervention including SMS with a computerised CVD risk evaluation and face-to-face counselling. The trials of interventions delivered by SMS alone or interventions delivering SMS to patients plus clinician training / decision support, reported little or no benefit on mean BP. The delivery of mobile phone-based interventions is inexpensive once systems are set up and previous analyses of such interventions in other fields have demonstrated cost effectiveness (Guerriero 2013; Lester 2010). If interventions were shown to be cost-effective the modest benefits achieved at low cost would be important if achieved across whole populations.

While many of the trials included components of the intervention delivered to healthcare providers as well as patients or delivered by other more resource-intensive means to patients, such as face-to-face counselling sessions with healthcare workers in addition to text messaging, only two out of seven of these reported clinically and statistically significant intervention benefits.

Implications for research

One trial at low risk of bias reported benefits on LDL cholesterol. It remains unclear why this intervention reported benefits whilst others with some apparently similar components did not. Given the heterogeneity of the interventions, future research should evaluate the effect of this intervention in other settings to provide greater certainty about the effects.

Trials involving self-monitoring and telemedicine support reported benefits but were at risk of bias. Further trials addressing methodological or reporting limitations are therefore needed. Trial results suggested that different means of providing the telemedicine support component may have different effects, which could usefully be evaluate by future trials.

The two interventions delivered by SMS alone were developed with input from users (Bobrow 2016; Tobe 2019). The intervention by Bobrow 2016 by targeted many of the barriers to adherence, which might be addressed using SMS. Nonetheless, the modest or absent benefit on mean BP and BP control is consistent with results of adherence interventions delivered by SMS for secondary prevention of CVD, HIV medication and diabetes (Adler 2017; Anglada-Martinez 2015; Farmer 2016). Adherence is influenced by a wide range of service and social factors, in addition to the individual-level factors like knowledge, motivation and skills (DiMatteo 2004; Julius 2009; Kardas 2013; Nieuwlaat 2014; Pound 2005; Vermeire 2001). Future adherence interventions should build on existing knowledge by considering the content of adherence intervention shown to be effective previously and by considering the broad range of factors influencing adherence that may be amenable to change. Future trials should target people most at risk of poor adherence and should exclude those known to be adherent.

For the indirect measures of adherence, the largest effect estimates related to those outcome measures reliant on participants' self-report. Where possible, future trials should prioritise including measures of adherence which are less subject to bias resulting from unblinded participants.

Finally, given the heterogeneity that exists between behaviour-change interventions, we believe that further high-quality adequately-powered trials of particular interventions would provide higher-quality evidence relating to the effectiveness, compared with evidence based on attempts to pool multiple smaller, lower-quality and potentially heterogeneous interventions and trials.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Bobrow 2016

Study characteristics	
Methods	**Design:** 3-arm, parallel RCT **Setting:** outpatient chronic disease services in a public sector clinic, Cape Town, South Africa **Duration of study:** 12 months
Participants	**Number randomised:** 1372; group 1 (control): 457; group 2 (informational SMS): 457; group 3 (interactive SMS): 458

Bobrow 2016 *(Continued)*

Number lost to follow-up/withdrawn: 176; group 1: 61 (reasons: 3 died; 2 pregnant; 14 lost contact; 12 moved; 25 unable to attend; 5 reason not given); group 2: 51 (reasons: 7 died; 2 pregnant; 7 lost contact; 11 moved; 23 unable to attend; 1 reason not given); group 3: 64 (reasons: 7 died; 5 pregnant; 2 participant decision; 7 lost contact; 14 moved; 29 unable to attend)

Number analysed: 1372; group 1: 457; group 2: 457; group 3: 458 (intention-to-treat analysis using all data available)

Mean age in years (SD): group 1: 54.7 (SD 11.6); group 2: 53.9 (SD 11.2); group 3: 54.2 (SD 11.6)

Age range: not stated

Gender (% women): group 1: 72; group 2: 72; group 3: 72

Proportion meeting criteria of 'primary prevention': 78.3% (unpublished information received from authors)

Proportion prescribed medication for prevention of CVD: 100%; prescribed BP-lowering medication was an inclusion criterion

Inclusion criteria: aged ≥ 21 years, diagnosed with hypertension by a clinician using local guidelines, prescribed BP-lowering medication, and with SBP < 220 mmHg and a DBP < 120 mmHg at enrolment. Eligible participants were attending the primary care clinic, resided in 1 of the 2 study communities and had regular access to a mobile phone (and were able to send SMS text messages or could do so with help of a relative)

Study enrolled only 1 member per household

Exclusion criteria: requiring specialist care for hypertension at a hospital (in secondary care), women who self-reported being pregnant or within 3 months postpartum, and people with very high BPs (SBP > 220 mmHg or DBP > 120 mmHg) who had symptoms suggestive of a hypertensive emergency or were otherwise acutely unwell (who were directly referred to the appropriate clinical service)

Interventions

Intervention: all participants received written information about hypertension and continued to receive care from the clinic

Group 2: 'informational SMS texting:' participants received: text messages to motivate collecting and taking medicines and to provide education about hypertension and its treatment. The messages were designed to address a range of common issues with adherence to and persistence with treatment. Additional reminders were sent when medicines were ready for collection or for scheduled clinic appointments

Group 3: 'interactive SMS texting' group: participants received: the same messages as the information-only group but could also respond to selected messages using free-to-user "please call me" requests. These generated an automated series of responses from the text message delivery system offering trial participants a number of options, including cancelling or changing an appointment and changing the timing and language of the text messages. The intervention was specifically designed to primarily focus on medication adherence, with only a few references other lifestyle modifications such as diet and physical exercise

Comparison: control group (group 1) received written information about hypertension and healthy living and continued to receive care from the clinic. The control group only received the texts sent to all trial participants, which were sent no more frequently than 1 text every 4 weeks. The messages were a welcome text, a text confirming enrolment, a text on a birthday and other text messages about participation in the trial.

How intervention was developed: the researchers iteratively designed, developed and tested 2 SMS text messaging-based interventions with clinical staff and participants with high BP working and living in low-income communities around Cape Town

Personalised intervention: some texts were personalised to include participants' first or chosen name. Information provided not personalised, but reminders of when medications were available for collection and dates of next appointment indicate some personalisation. Additionally, the 'interactive SMS texting' group (group 3) could request further interactions

Bobrow 2016 *(Continued)*

	Frequency and duration of intervention receipt: messages sent weekly at a time selected by participant. Intervention duration: 12 months
Outcomes	**Primary outcomes:** SBP (mean); proportion of participants achieving a mean SBP < 140 mmHg and a mean DBP < 90 mmHg. Measured at 12 months' post-randomisation **Secondary outcomes:** medication adherence: 'proportion of days of medication covered' (the proportion of participants with ≥ 80% of days covered with BP-lowering medication from prescribing and dispensing data routinely recorded in the clinical record, pharmacy record and Chronic Dispensing Unit record); self-reported adherence to medication using a visual analogue scale (score range, 5 – 10); health status measured with the EuroQol Group 5-Dimension Self-Report Questionnaire; self-reported satisfaction with treatment **Process outcomes:** knowledge about hypertension was measured, but not reported in trial paper **Adverse events:** protocol stated recording of those which might reasonably occur as a consequence of the trial and adverse events that might be reasonably related to text messaging including hand or finger pain, or involvement in an accident as a result of sending or receiving a text
Notes	**Funding source:** trial supported by the Oxford Centre of Excellence in Medical Engineering funded by the Wellcome Trust and the Engineering and Physical Sciences Research Council. Dr Farmer is a senior NIHR investigator, and Drs Farmer and Tarassenko are supported by funding from the NIHR Oxford Biomedical Research Center. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript **Conflicts of interest:** none declared

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "participants are randomised using a secure, remote, web-based computer schedule within one week of recruitment [...] minimisation procedure [was] overseen by an independent statistician."
Allocation concealment (selection bias)	Low risk	Quote: "A software algorithm assigned participants independently of the research team."
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants cannot be blinded due to nature of intervention. However, "research staff and clinic staff remain blind to the allocated treatment group."
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Researchers and clinicians were not aware of randomization assignment, were trained not to ask patients about the content of messages."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Participants unable to be blinded, and some outcomes were self-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	87% follow-up rate, no evidence of differential follow-up, ITT analysis accounting for missing data
Selective reporting (reporting bias)	Unclear risk	Outcomes reported as planned in protocol (the only outcome reported in protocol that was not reported in trial paper was 'hypertension' knowledge). However, this trial began recruiting in June 2012, but details of the protocol were not registered until December 2013. We therefore could not be certain what was planned before the trial began

Bobrow 2016 *(Continued)*

Other bias	Low risk	N/A

Choudhry 2018

Study characteristics	
Methods	**Design:** 2-arm, cluster RCT **Setting:** Recruited from 14 primary care practice sites of a large multi-specialty group practice in Massachusetts USA **Duration of study:** 12 months
Participants	**Number randomised:** 4078 (NB protocol says 4076 randomised); intervention: 2038; control: 2040 **Number lost to follow-up/withdrawn:** No loss for adherence. 15.7% participants were missing clinical outcome data **Number analysed:** 4078. Multiple imputation used to handle missing clinical outcome data **Mean age in years (SD):** 59.8 (11.6); intervention: 60.4 (11.7); control: 59.2 (11.5) **Age range:** Not reported **Gender (% women):** 45.1%; intervention: 45.3%; control: 45% **Proportion meeting criteria of 'primary prevention':** 98.1% (79 with acute coronary syndrome). (NB 3.6% had heart failure) **Proportion prescribed medication for prevention of CVD:** 100% prescribed medication but some were only taking glucose-lowering agents – number unknown **Inclusion criteria**: At least 18 years and < 85 years. Receiving care at the study primary care practice. Receiving health insurance from 1 of 4 large insurers. Diagnosis of hyperlipidaemia, hypertension, or diabetes based on having filled a relevant prescription medication (statins, antihypertensives, or oral glucose-lowering agents). Poor or worsening disease control for at least 1 of these conditions evaluated using the most recent laboratory or blood pressure values in the electronic health record at the time of enrolment. < 80% adherence to the prescribed therapy for their uncontrolled condition and < 80% average adherence to all eligible study drugs, assessed using prescription claims data **Exclusion criteria:** People with less than 6 months of continuous enrolment in the health plan prior to randomisation. No available telephone contact information
Interventions	**Intervention:** an individually-tailored telephone consultation conducted by a staff clinical pharmacist who used a semi-structured guide to confirm the participant's treatment regimen, engaged them in sharing potential barriers to adherence or other factors that may be contributing to poor disease control, discussed the participant's readiness to modify behaviours, and worked with the participant to develop a shared plan to improve adherence and disease control. The Patient Activation Measure questionnaire was used to assess knowledge, skills, and confidence to manage one's health and health care. Strategies were tailored to participants' activation level and identified adherence barriers and included: structured consultation reports sent to participants' primary care physicians with recommendations for modifying treatment regimens and co-ordinating care, strategies to promote adherence including text messages (as reminders and motivational support) and pillboxes, and follow-up consultations. Mailed progress reports were sent at 6 and 9 months after randomisation, providing personalised information about disease control and medication adherence **Comparison:** Usual care: clinical pharmacists were available for consultation upon request by a participant's primary care provider, but outreach was not done routinely. Usual-care clinical pharmacists were not trained in the motivational interviewing method used as part of the intervention, did not have access to detailed adherence information for each participant or activation levels, nor did they have the ability to offer text messages or progress reports **How intervention was developed:** Structure of telephone consultations developed by the study team using brief negotiated interviewing **Personalised intervention:** Strategies were personalised based on activation level and identified adherence barriers, e.g. content and frequency of text messages and whether participants received pillboxes **Frequency and duration of intervention receipt:** 12-month duration

Choudhry 2018 *(Continued)*

Outcomes	**Primary outcomes:** Proportion with good disease control for all eligible conditions. Good control was defined at systolic blood pressure < 150 mgHg if age ≥ 60 and < 140 mgHg if age < 60; HbA1c < 8; LDL < 100 mg/dl (for ASCVD risk > 20%), LDL < 130 mg/dL (for ASCVD risk 10% - 20%), or LDL < 160 mg/dL (for ASCVD risk < 10%). Mean LDL and systolic BP. Using the electronic health-record values recorded closest to the end of 12 months follow-up **Secondary outcomes:** Medication adherence for hyperlipidaemia and hypertension at 12 months. Assessed using prescription claims data and measured as the mean proportion of days covered (PDC) over the 12 months after randomisation. Adherence was measured only for medications that qualified a participant for inclusion the study beginning at the time of randomisation **Process outcomes:** Number of participants who completed the telephone consultations, received text messages, pillboxes and progress reports **Adverse events:** N/A **Other outcomes (not for extraction):** Proportion with good disease control for at least 1 eligible condition. Absolute change in HbA1c. Primary outcomes adjusted for age and race/ethnicity. Complete-case analysis of all non-missing clinical outcomes. As-treated analysis. Overall mean medication adherence. Subgroup analyses of adherence according to age, sex, race/ethnicity, baseline adherence levels and number of conditions and medications that identified the participants for the study. Rates of healthcare use measured using administrative-claims data including all-cause emergency department visits, physician office visits, and hospitalisations during follow-up
Notes	ClinicalTrials.gov NCT02512276 **Funding source:** National Heart, Lung, and Blood Institute, National Institute of Health, to Brigham and Women's Hospital **Conflicts of interest:** Dr Choudhry has received unrestricted research grants to study medication adherence from Sanofi, AstraZeneca, Merck, and Medisafe. Dr Lauffenburger has received salary support for unrestricted research grants from Sanofi and AstraZeneca

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Practice sites were categorized into blocks based on their size and whether, prior to randomization, clinical pharmacists at the sites offered disease management counseling directly to patients. Within the resultant 4 blocks, practices were randomized in a 1:1 ratio to intervention or control using a random number generator"
Allocation concealment (selection bias)	Low risk	Clusters randomised before participant recruitment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of study participants or clinical personnel
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Study investigators and data analysts remained blinded until all follow-up data were obtained and the primary analytic strategies were finalized". Comment: Clinical outcomes obtained from electronic health records
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Cinical data was missing for some (15.7%) patients. Accordingly, we used multiple imputation with 20 imputations. This approach achieved in-range values and a 99% relative efficiency. All analyses were conducted on each imputed dataset."

Choudhry 2018 *(Continued)*

Selective reporting (reporting bias)	Low risk	Study protocol is available and outcomes are reported in the prespecified way. Trial registered prior to recruitment (clinicaltrials.gov/ct2/show/NCT02512276).
Other bias	Low risk	Selective cluster recruitment: Quote: "intervention patients were slightly older and less likely to be of white race/ethnicity but were otherwise similar to usual care patients, including with respect to baseline levels of disease control and medication adherence, with standardized mean differences less than 0.1"

Gulayin 2019

Study characteristics	
Methods	**Design:** 2-arm, cluster RCT **Setting:** 10 public primary care clinics in the provinces of Chubut, Corrientes and La Rioja, Argentina **Duration of study:** 12 months
Participants	**Number randomised:** Total: 357; intervention: 179; control: 178 **Number lost to follow-up/withdrawn:** Total: 10 (7 LTFU, 3 died); intervention: 3 (1 LTFU, 2 died); control: 7 (6 LTFU, 1 died) **Number analysed:** Total: 347; intervention: 176; control: 171 **Mean age in years (SD):** intervention: 56.8 (8.4); control: 56.0 (8.0) **Age range:** Not reported **Gender (% women):** intervention: 41.3%; control: 27.5% **Proportion meeting criteria of 'primary prevention':** intervention: 74.3%; control: 62.9% **Proportion prescribed medication for prevention of CVD:** No participant at baseline; statin therapy at baseline was an exclusion criterion. At 6 months, prescription of statins at an appropriate dose; intervention: 44.4%; control 7.3%. At 12 months, intervention: 49.1%; control: 7.7% **Inclusion criteria:** Study clinics were eligible if they were affiliated with the Remediar programme, located in a poor urban area according to 2010 census data, have ≥ 800 outpatient adult visits each month (to ensure recruitment of enough participants); physician visits and statins were available free-of-charge to patients at the point of care and they showed good performance. The minimum distance between clinics was 10 km (different catchment area) and they did not share health professionals (to minimise intervention bias) Patients were eligible if they were aged 40 - 74 years, were receiving care at participating PCCs, and met at least 1 of the following criteria: medical history of arteriosclerotic CVD (defined as acute coronary syndrome, history of myocardial infarction, stable or unstable angina, coronary revascularisation, stroke, or transient ischaemic attack presumed to be of atherosclerotic in origin or revascularisation); high CVD risk according to the WHO charts adapted by the National Ministry of Health (estimated 10-year CVD risk ≥ 20%); LDL-c level ≥ 190 mg/dL; or Type 2 diabetes **Exclusion criteria:** Patients were excluded if at least 1 of the following conditions were present: statin treatment, pregnancy, bed-bound, inability to give informed consent, history of end-stage chronic kidney disease treated with dialysis, HIV/AIDS, alcohol or drug abuse, or active tuberculosis
Interventions	**Intervention:** the intervention included 3 main components: (1) an intensive 2-day training workshop followed by certification at the outset; followed by (2) 3 quarterly educational outreach visits (EOVs); and (3) a mobile health (mHealth) application installed on the physician's smartphones to facilitate evidence-based and guideline-driven decision aids to improve patient management The 2-day workshop was held at the Institute for Clinical Effectiveness and Health Policy and conducted by a cardiologist and an internal medicine specialist. The topics included in the training sessions were global CV risk assessment and management; diagnosis, treatment, and monitoring of patients with dyslipidaemia; the chronic care model components; and management of adherence issues in patients with chronic diseases. The EOVs were also performed by cardiologists and internal medicine specialists and consisted of onsite face-to-face encounters with local physicians. Based on data from local practice and CPG practical exercises, the specialists gave individual feedback, assisted with the possi-

Gulayin 2019 *(Continued)*

	ble needs of practitioners at the clinics, and identified barriers that prevented appropriate prescription (e.g. side effects of statins, barriers for chronic treatment adherence). All physicians had the mHealth application installed on their phones during the study, which were used during the EOVs. It included evidence-based statin use recommendations shown on screen after completing information for CVD risk estimation In addition, the following support tools were used in the intervention group: (1) a web-based platform designed to send weekly SMS messages to promote healthy lifestyles, regular visits to the clinic, and to improve medication adherence for study participants; and (2) onsite training to pharmacist assistants given at the first EOV in each intervention clinic, focused on participant counselling on medication adherence. Additionally, educational flyers were distributed to be displayed in the pharmacy room **Comparison:** Usual care at clinics consists of mostly unscheduled appointments with a primary care physician on participant's demand. All clinics in the network provide ambulatory drugs free-of-charge at the point of care and most of the physicians, irrespective of the assignment, have received previous training in global cardiovascular risk management by trainers of the Ministry of Health. In addition, all clinics were provided with educational flyers and written material to be displayed at the PCCs, including charts with the CPG on the use of statins **How intervention was developed:** Development of SMS messaging not described **Personalised intervention :** SMS messages were not personalised **Frequency and duration of intervention receipt:** Weekly SMS messages. Duration not stated. Study period was 12 months
Outcomes	**Primary outcomes:** Net change in LDL-c levels from baseline to 12 months. (In protocol but not in the paper: proportion of participants with moderate and high CVD risk who have reduced their LDL-c by 30% and 50% respectively) **Secondary outcomes:** Self-reported treatment adherence among treated participants using the Morisky-Green questionnaire **Process outcomes:** N/A **Adverse events:** N/A **Other outcomes (not for extraction):** Proportion of participants with high CVD risk who were on statins and receiving an appropriate dose. Net change in 10-year CVD Framingham risk score before. Mean annual number of follow-up visits to the PCC for high CVD risk. Subgroup analyses by diabetes status
Notes	ClinicalTrials.gov NCT02380911 **Funding source:** International Atherosclerotic Society – Pfizer grant **Conflicts of interest:** No financial disclosures were reported by the authors

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The 10 selected PCCs fulfilling the inclusion criteria were randomised to either the intervention or the control group: five PCCs to the intervention and five to the control group. Randomisation was stratified by province and it was conducted at the data management centre at the Institute for Clinical Effectiveness and Health Policy".
Allocation concealment (selection bias)	Low risk	Clusters randomised before participant recruitment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of study participants or clinical personnel
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Not clear whether study nurses collecting outcome data or data analysts/investigators were blind to the intervention

Gulayin 2019 *(Continued)*

Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Participants were not blinded to the intervention assignment. Adherence data were from a participant questionnaire
Incomplete outcome data (attrition bias) All outcomes	Low risk	Differences in means among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	High risk	Not all of the secondary outcomes have been reported. The protocol outcomes include "proportion of patients with moderate and high CVD risk who have reduced their LDL-c by 30% and 50% respectively" and "incremental cost-effectiveness ratio per case receiving an appropriate dose". These outcomes are not mentioned in the paper. Level of treatment adherence is only reported as "no difference". No data are provided
Other bias	Low risk	Selective cluster recruitment: Quote: "all analyzed [baseline] variables were balanced except for the mean diastolic blood pressure, which was higher in the control group." Comment: Mean LDL-cholesterol at baseline was similar between groups

He 2017

Study characteristics	
Methods	**Design:** cluster RCT **Setting:** 18 primary healthcare centres within a national public system in Argentina, providing free healthcare to low-income, uninsured people **Duration of study:** 18 months
Participants	**Number randomised:** 1432 hypertensive people; intervention 743; control 689 **Number lost to follow-up/withdrawn:** 75; intervention 34; control 41 **Number analysed:** 1357; intervention 709; control 648 **Mean age in years (SD):** 55.8; intervention 56.1 (13.6); control 55.5 (13.0) **Age range:** not stated **Gender (% women):** 53%; intervention 52.6%; control 53.4% **Proportion meeting criteria of 'primary prevention':** without major CVD: MI or stroke - intervention 87.3%; control 91.0% **Proportion prescribed medication for prevention of CVD:** at baseline – intervention 86%; control 83.5% **Inclusion criteria:** Eligibility for centres were an affiliation with the Remediar+Redes Program, location in a poor urban areas and employment of CHWs in addition to general practitioners and nurses. From those eligible, 18 were recommended by the Remediar+Redes Program based on their geographic distribution, their willingness to participate and their previous experience collaborating with the co-ordinating centre. From the protocol - 1000+ outpatient visits each month, minimum 10 km between selected centres, high number of prescriptions of antihypertensive medications, performs blood draws on patients when appropriate Eligibility criteria for participants were uncontrolled BP (systolic ≧ 140 mmHg or diastolic ≧ 90 mmHg, or both, on at least 2 separate screening visits), age ≧ 21 years, uninsured and receiving primary care from the participating centres, and spouses (with/without hypertension) and/or adult hypertensive family members aged ≧ 21 years living in the same household who were willing to participate in the study. Hypertensive participants and spouses/family members must be available for the first baseline nurse visit. Index participant has a cell phone that receives text messages. Home is within 10 km of the clinic **Exclusion criteria:** (from the protocol) No spouse or another adult family member in the household. Plan to move from the neighbourhood in the next 2 years. Pregnant women or planning to become pregnant in the next 2 years. Bed-bound. Arm circumference > 50 cm.

He 2017 *(Continued)*

Interventions	**Intervention:** CHW-led home-based intervention, physician education and BP feedback and weekly text-messaging CHWs visited participants' homes monthly for the first 6 months and every other month thereafter. They started with a 90-minute visit when all family members were available to discuss general knowledge about hypertension prevention and treatment. During subsequent 60-minute visits they provided tailored counselling to participants and their families on lifestyle modification, home BP monitoring, and medication adherence skills. They reviewed specific strategies for lifestyle modification and encouraged participants to adopt strategies most suitable for their individual needs. They focused on goal setting, problem-solving, social support, and maintaining motivation during challenging situations. Participants with hypertension were given an automatic home BP monitor and 7-day pill organizer. CHWs helped participants schedule appointments with primary care physicians and delivered antihypertensive medication to their homes if they did not have access to transportation Primary care physicians were trained in standard treatment algorithms for stepped-care BP management based on clinical guidelines. Feedback was given to physicians, based on home BP monitoring data, to encourage medication adjustment when needed Individualised text-messages to promote lifestyle changes and reinforce medication adherence were sent out weekly to participants' mobile phones by an eHealth platform. Messages were based on hypertension status and perceived barriers to behavioural change identified during CHW home visits and consisted of motivational statements and behaviour-change techniques to reinforce in-person education interventions. CHWs also collected information on participants' receipt of text messages **Comparison:** Neither physicians nor CHWs were trained to conduct study interventions. Participants did not receive CHW home visits, home BP monitors, or text messages. Participants were encouraged to follow the clinical visit schedule of the Remediar+ Redes Program: monthly among participants after pharmacological treatment initiation and every 3 - 6 months among participants who had controlled BP **How intervention was developed:** Intervention addressed system, provider and participant barriers to hypertension prevention and control by integrating individual strategies previously proven effective **Personalised intervention:** Yes; text messages and CHW strategies were tailored to perceived barriers to behavioural change identified during CHW home visits **Frequency and duration of intervention receipt:** weekly text messaging. 1 - 2 monthly home visits. 18 months duration
Outcomes	**Primary outcomes:** Change in systolic and diastolic blood pressure from baseline to end follow-up in participants with hypertension. Proportion of participants with controlled hypertension (BP < 140/90 mmHg) Secondary outcomes: self-reported antihypertensive medication adherence using the Morisky Medication Adherence Scale; cost per additional percentage of hypertension controlled **Process outcomes:** Percentage of planned CHW home-based interventions completed. Percentage of anticipated home BP measurements completed. Percentage of schedule text-messages sent. Percentage of participants reporting receipt of weekly messages **Adverse events:** Hypotension, syncope and injurious falls were queried at study nurse visits **Other outcomes (not for extraction):** Intensification of antihypertensive medication; weight change over the 18-month intervention; change in systolic and diastolic BP among normotensive participants
Notes	**Funding source:** National Heart, Lung, and Blood Institute of the National Institutes of Health, award number U01HL114197 and partially by the National Institute of General Medical Sciences of the National Institutes of Health, award number P20GM109036 **Conflicts of interest:** No conflicts of interest reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Cluster randomisation was stratified by geographic region and conducted at the data co-ordinating centre at Tulane University. The randomisation schedules were generated using PROC PLAN in SAS software
Allocation concealment (selection bias)	Unclear risk	Not described but likely to be low, as clusters randomised before recruitment of participants

He 2017 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Study physicians, CHWs, and participants were not blinded to intervention assignment."
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Quote: "Study outcomes were collected by nurses who were not involved in the intervention". Comment: Not clear if they were blind to it
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Participants were not blinded to the intervention. Adherence data were self-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	94.8% completed 18-month follow-up. Multiple imputation was conducted as a sensitivity analysis and did not change results
Selective reporting (reporting bias)	Low risk	The study protocol is available and all planned analyses are reported. Trial registration pre-dates recruitment (clinicaltrials.gov/ct2/show/NCT01834131).
Other bias	Unclear risk	Selective cluster recruitment - all hypertensive patients on the clinic lists were assessed for eligibility. Quote: "In general baseline characteristics were balanced between intervention and control groups. However, the intervention group had a slightly higher proportion of individuals with self-reported major cardiovascular disease and hypercholesterolemia, as well as higher levels of mean systolic and diastolic BP, compared with the control group."

Liu 2015

Study characteristics	
Methods	**Design:** 2-arm, parallel RCT **Setting:** employees of work units (places of employment) who had been allocated to have a medical examination at the health management centre of a hospital in Guangzhou, China **Duration of study:** 1 year
Participants	**Number randomised:** 589; intervention: 238; control: 351 **Number lost to follow-up/withdrawn:** 162 (intervention: 75; reasons: not stated; control: 87; reasons: not stated) **Number analysed:** 589, intervention: 238; control: 351 (missing data imputed) **Mean age in years (SD):** intervention: 58.7 (SD 8.9), control: 61.8 (SD 8.8) **Age range:** not stated **Gender (% women):** intervention: 41.6; control: 41.9 **Proportion meeting criteria of 'primary prevention':** 100%; inclusion criteria included having no known CVD **Proportion prescribed medication for prevention of CVD:** not reported. Authors contacted for further information and the data for those prescribed medication, but we received no response

Liu 2015 *(Continued)*

	Inclusion criteria: aged 45 – 75 years, without known CVD, willing to participate in the programme **Exclusion criteria:** history of mental abnormalities; difficulty in communication, such as reading or answering the questionnaire; unable to understand the aim of this study; currently participating in another clinical trial or had done so within the previous 6 months
Interventions	**Intervention:** participants in the intervention group received a computerised CVD risk evaluation, follow-up phone calls and text messages targeting reducing the CVD risk in addition to the usual medical examination. The plan included guidance of healthy lifestyle, improvement targets for risk factors and drug treatment goals for those being treated. Participants also received a 15-minute face-to-face counselling with a trained field health worker when they enrolled to the study **Comparison:** participants in the control group received the annual medical examination with a usual medical report. This report included the results of physical examination and the normal values of the indicators **How intervention was developed:** authors stated, "we developed a mobile phone-based intervention program to reduce CVD risk, which was assessed by the Chinese cardiovascular disease risk assessment method." **Personalised intervention:** yes; individualised electronic health prescription software (IEHPS) calculated participants' overall risk of CVD in the next 10 years which informed participants' individualised intervention plan **Frequency and duration of intervention receipt:** frequency of phone calls and text messages depended on participants' individual 10-year CVD risk. Phone calls (length 5 – 8 minutes) ranged from twice a month to once a week, text messages ranged from once a month to once a week **Duration**: 1 year
Outcomes	**Primary outcomes:** LDL-C, TC, HDL-C, SBP, DBP. All measured at 1-year post-randomisation. Medical outcomes were presented for entire sample, which included participants not taking medication for primary prevention of CVD. We have contacted authors requesting trial data for those participants taking medication for primary prevention of CVD **Secondary outcomes:** none reported **Process outcomes:** none recorded **Adverse events:** none recorded
Notes	**Funding source:** Guangdong Provincial Department of Science and Technology (grant No. 2009A030301003) and the Bureau of Health of Guangzhou Municipality (grant No. 2008-ZDa-05) **Conflicts of interest:** none declared

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomization was done via a computerized procedure."
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Neither participants nor investigators were masked to group assignment."

Liu 2015 *(Continued)*

Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Assessments by medical students; not stated whether they were blinded
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "27.5% of participants failed to attend the follow-up. Participants who were lost to follow-up were more likely to be younger, male, current smokers and have a higher level of TC than those who were included in the follow-up."
Selective reporting (reporting bias)	Unclear risk	Protocol not found. Trial appears to have been registered after recruitment began in October 2012 (chictr.org.cn/hvshowproject.aspx?id=7953)
Other bias	Low risk	N/A

Logan 2012

Study characteristics	
Methods	**Design:** 2-arm, parallel RCT **Setting:** clinics in metropolitan Toronto, Canada **Duration of study:** 1 year
Participants	**Number randomised:** 110; intervention: 55; control: 55 **Number lost to follow-up/withdrawn:** 6; intervention group: 2 (reasons: 2 refused BP assessment); control group: 4 (reasons: 3 refused BP assessment; 1 died) **Number analysed:** 105; intervention group: 54; control group: 51 **Mean age in years (SD):** intervention group: 62.7 (SD 7.8); control group: 63.1 (SD 9.0) **Age range:** not stated **Gender (% women):** intervention group: 51; control group: 38 **Proportion meeting criteria of 'primary prevention':** intervention group: 79.9%; control group: 78.1%. Paper reported proportion with prior CVD event by CVD event, possible that the same participants had > 1 type of event, so percentage stated was minimum estimate of participants meeting criteria of primary prevention **Proportion prescribed medication for prevention of CVD:** hypertensive drugs: intervention group: 89.1%; control group: 89.1%; lipid-lowering drugs: intervention group: 69.1%; control group: 70.9%; aspirin: intervention group: 54.5%; control group: 58.2%. We contacted authors to request data for those prescribed medication, but had no response **Inclusion criteria:** aged ≥ 30 years, with diabetes mellitus, with uncontrolled systolic hypertension, defined as a mean daytime SBP of ≥ 130 mmHg on ambulatory BP monitoring **Exclusion criteria:** those with severe or end-stage organ disease (liver, kidney, heart and lung), history of diabetic ketoacidosis, any illness with expected survival < 1 year, severe cognitive impairment, mental illness or disability, clinically-significant cardiac arrhythmia, symptomatic orthostatic hypotension, or were pregnant, unsuitable for participation in the opinion of their primary care physician or not fluent in English

Logan 2012 *(Continued)*

Interventions	**Intervention:** participants received custom software application running on a BlackBerry smartphone (Research In Motion, Inc, Waterloo, ON, Canada) that was paired with a Bluetooth-enabled home BP monitoring device. BP readings were automatically transmitted by the smartphone to application servers, which processed the information for trends and applied decisions rules. The reporting and alerting component of the system sent a self-care message to the screen of the participant's smartphone immediately after each reading. Messages related to the control of hypertension were based on care paths defined by running means of transmitted readings. On the day before the clinic visit to their physician, participants called a dedicated telephone number to initiate the automated process to fax a 1-page participant summary report to their physician. Self-care support participants were taught how to use the telemonitoring system, review past readings on their smartphone and the study-specific website (these activities were optional), and generate a 1-page participant summary report. They were instructed to take their smartphone to all doctor visits **Comparison:** participants in both groups were taught how to measure their BP correctly, instructed to measure their BP 2 days per week twice in the morning and twice in the evening, provided with a validated home BP-monitoring device with appropriate-sized upper arm cuff, and given a booklet with detailed information on the self-measurement of BP, treatment of hypertension and goals of therapy. Their primary care physician was given an outline of the study's objectives and BP treatment goal, asked to provide relevant medical information and given a copy of the 24-hour ambulatory BP monitoring report. In both groups, treatment decisions, including medication adjustments and changes in lifestyle, were made by the participant's primary care physician. The control group did not received feedback via smartphone **How intervention was developed:** system developed using an iterative process based on feedback from users. A pilot study was undertaken to assess the system's effectiveness in improving BP control in people with diabetes with uncontrolled hypertension, its acceptability to users and the reliability of home BP measurements **Personalised intervention:** information sent via smartphone was personalised in that it was based on participants' own BP readings **Frequency and duration of intervention receipt:** participants were instructed to measure their BP 2 days per week twice in the morning and twice in the evening, and a self-care message was sent to the participant's smartphone immediately after each reading. **Duration**: 1 year.
Outcomes	**Primary outcomes:** mean ambulatory SBP and DBP; proportion achieving guideline recommended target of BP < 130/80 mmHg. Measured at 1 year' post-randomisation. The medical outcomes are presented for entire sample, which included participants not taking medication for primary prevention of CVD. We contacted authors requesting trial data for those participants taking medication for primary prevention of CVD, but had no response **Secondary outcomes:** none reported **Process outcomes:** adherence rate with home BP measurement schedule (% taking a minimum of 8 readings per week) **Adverse events:** none recorded
Notes	**Funding source:** the Heart and Stroke Foundation of Ontario (ESA 5970) was the sole source of funding for this project and was not involved in any aspect of the study **Conflicts of interest:** JAC received funding from Research In Motion, Inc. (makers of the Blackberry mobile telephones) through the National Science and Engineering Research Council Strategic Network Grant Program. PGR received reimbursement of expenses from Research In Motion, Inc., to attend a healthcare advisory meeting

Risk of bias

Bias	Authors' judgement	Support for judgement

Logan 2012 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "Group allocation schedule was based on blocks of 4 and 6 patients randomly arranged and administered by a person not directly involved in the study."
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants cannot be blinded due to nature of intervention. Unclear whether personnel were blinded
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Low risk	> 90% follow-up, no evidence of differential follow-up
Selective reporting (reporting bias)	Unclear risk	According to trial registry entry (clinicaltrials.gov/ct2/show/NCT00717665), the trial was registered after the first participant was randomised
Other bias	Low risk	N/A

Márquez Contreras 2019

Study characteristics	
Methods	**Design:** Cluster RCT **Setting:** 4 primary care centres, Huelva, Spain **Duration of study:** 12 months
Participants	**Number randomised:** Total: 154; intervention: 77; control: 77 **Number lost to follow-up/withdrawn:** Total: 6; intervention: 4 (2 technical problems with the MEMS; 1 moved away; 1 long hospitalisation); control: 2 (failed to attend follow-up visits) **Number analysed:** Total: 148; intervention: 73; control: 75 **Mean age in years (SD):** Overall: 57.5 (9.9); intervention: 57.7 (9); control: 57.08 (10) **Age range :** not stated **Gender (% women):** Overall: 52.02%; intervention: 52.1%; control: 52% **Proportion meeting criteria of 'primary prevention':** Intervention: 2.73% IHD, 4.1% stroke; control: 2.66% IHD, 1.33% congestive heart failure, 4% stroke **Proportion prescribed medication for prevention of CVD:** 100% **Inclusion criteria:** Outpatients aged > 18 years; diagnosed with mild-moderate hypertension (criteria ESH-ESC 2013); receiving pharmacological treatment with an antihypertensive tablet at least 1 month before inclusion in the study **Exclusion criteria:** Pregnant or lactating women; patients whose pathological situation could interfere with the development of the study (AMI, cognitive impairment, terminal illness etc); participants in other research studies; hypertensive patients who had a partner taking the same antihypertensive medication

Márquez Contreras 2019 *(Continued)*

Interventions	**Intervention:** A free APP was installed on the participants' mobile phones with the aim of promoting health education and reminding them of both appointments and medication intake time. They received instructions from their physician on how to use the APP and were given the operating instructions of the APP in writing. The App allows you to record personal data, recommended BP levels as objectives, record the doctor's advice about the prescribed treatment, the posology, set reminder alarms, set a calendar of appointments or events, and record the results of the BP measurement **Comparison:** Usual intervention for high blood pressure: 6-monthly blood pressure control, annual control of therapeutic adherence, annual analysis and biannual electrocardiogram **How intervention was developed:** The APP is called ALERHTA: it has been specially created for the Hypertensive Club of the Spanish Society of Hypertension (SEH-LELHA), it is easily accessible and free to obtain **Personalised intervention:** No **Frequency and duration of intervention receipt:** APP available throughout the 12 months follow-up providing daily reminders
Outcomes	**Primary outcomes:** Mean change in systolic and diastolic blood pressure over 12 months. Percentage of participants with controlled BP (< 140 and 90 mmHg) **Secondary outcomes:** Daily adherence: percentage of participants who took antihypertensive drugs correctly on 80% - 100% of days. Measured using a Medication Event Monitoring System (MEMS) to electronically monitor when the drug container was opened **Process outcomes:** None recorded**Adverse events:** None recorded **Other outcomes (not for extraction):** Other measures of adherence: global percentages of doses taken, percentage of doses taken at the prescribed time (between 7 and 9 o'clock), percentage of therapeutic cover assuming a 24-hour effect of the drugs and adherence patterns
Notes	**Funding source:** The study is supported by institutional grant PI-0291-2014 and grant W1203903 **Conflicts of interest:** The authors and CMRO peer reviewers on this manuscript have no relevant financial or other relationships to disclose

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Cluster randomization was performed. Researchers were randomized, being their patients assigned to the control or intervention group. The randomization was carried out in a centralized manner, by an independent person and using random number tables."
Allocation concealment (selection bias)	Low risk	Clusters randomised before participant recruitment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of study participants or investigators, who were also the physicians managing the patients
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Insufficient information provided, although there was no blinding of study investigators
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Low risk	96% follow-up rate. Differences among missing outcomes not enough to have a clinically-relevant impact on observed effect size

Márquez Contreras 2019 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No published study protocol. States trial was registered, unclear whether this was prior to recruitment
Other bias	Unclear risk	Selective cluster recruitment - adherence at baseline not measured. No evidence of a difference in blood pressure at baseline

McManus 2018

Study characteristics	
Methods	**Design:** 3-arm parallel RCT **Setting:** 142 general practices, UK **Duration of study:** 12 months
Participants	**Number randomised:** Total 1182; telemonitoring: 393; usual care: 394 **Number lost to follow-up/withdrawn:** Total: 179 (174 lost to follow-up + 5 systolic BP not available); telemonitoring: 63+3; usual care: 44+2 **Number analysed:** For primary study outcome of systolic BP - Total:1003; telemonitoring: 327; usual care: 348 **Mean age in years (SD):** Intervention (telemonitoring): 67.0 (9.3); Usual care: 66.8 (9.4) **Age range:** Not reported **Gender (% women):** Intervention (telemonitoring): 47%; usual care: 47% **Proportion meeting criteria of 'primary prevention' :** MI 2%; CABG, angioplasty or stent 4%; Stroke 2% **Proportion prescribed medication for prevention of CVD:** 100% **Inclusion criteria:** Age > 35 years, diagnosis of hypertension, taking ≤ 3 antihypertensive agents, blood pressure not controlled below 140/90 mmHg, on stable antihypertensive medication for at least 4 weeks before randomisation **Exclusion criteria:** Orthostatic hypotension, atrial fibrillation, dementia, chronic kidney disease of grade 4 or worse or chronic kidney disease with proteinuria
Interventions	**Intervention:** Telemonitoring: medication review with own GP. Taught to use a validated automated electronic sphygmomanometer (Omron M10-IT). They were asked to monitor their own blood pressure in their non-dominant arm, twice each morning and evening, for the first week of every month using standard recommendations and their GPs were asked to use the self-monitored measurements for titration of antihypertensive medication. Participants were trained to send readings via a simple free SMS text-based telemonitoring service with web-based data entry back-up. The telemonitoring system incorporated an algorithm that alerted participants to contact their surgery in the light of very high or very low readings, reminded them if insufficient readings were transmitted, prompted them to make contact with their practice if their average blood pressure was above target, and presented readings to attending clinicians via a web interface. This secure web page automatically calculated mean blood pressure for each monitoring week, highlighted very high or very low readings, and presented a graphical display of blood pressure measurements. Attending clinicians were asked to review blood pressure readings on a monthly basis. **Comparison:** Usual care: medication review with own GP at baseline and thereafter managed with titration of antihypertensive treatment based on clinic blood pressure measurements at the discretion of their attending healthcare professional **How intervention was developed:** Not reported **Personalised intervention:** The telemonitoring system prompted participants to contact their GP if average blood pressure was above target or they had a very high or very low reading **Frequency and duration of intervention receipt:** 12 months. Used twice daily for 1 week each month
Outcomes	**Primary outcomes:** Clinic measured systolic and diastolic blood pressure (adjusted for baseline covariates) at 12 months. Cardiovascular events **Secondary outcomes:** self-reported adherence (Medication Adherence Rating Scale); quality of life (EQ-5D-5L). Cost effectiveness to be reported separately **Process outcomes:** N/A

McManus 2018 *(Continued)*

	Adverse events: side-effects, anxiety **Other outcomes (not for extraction):** Blood pressure at 6 months; Medication prescription (number and defined daily dose); weight and waist circumference; lifestyle factors; Sensitivity analyses to examine the robustness of the results using different approaches to obtaining mean blood pressure and replace missing values; subgroup analysis for age, sex, BP target, baseline BP, deprivation, history of CVD. Qualitative sub-studies to be reported separately
Notes	**Trial identifier:** ISRCTN 83571366 **Funding source:** National Institute for Health Research (NIHR) Programme grant (RP-PG-1209-10051), and NIHR Professorship awarded to RJM, the Chief Investigator (NIHR-RP-R2-12-015). **Conflicts of interest:** "The blood pressure monitors used in this study were provided free of charge by Omron Healthcare UK Ltd. FDRH received research support for a trial of heart failure diagnosis from Roche Diagnostics through the supply of BNP assays in 2010–11. All other authors declare no competing interests." **Note:** this was a 3-armed trial. Third arm (not extracted): self-monitoring of blood pressure 1 week a month as for the telemonitoring group. A simple colour chart was used to train participants to attend their practice for blood pressure checks in the light of very high or very low readings. At the end of each monitoring week they were asked to record their readings on paper and send them for review to their practice

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Eligible and willing participants were randomly assigned (1:1:1), using a secure web-based system, with stratification by practice and minimisation on baseline blood pressure, sex, and blood pressure target"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Neither participants nor investigators were masked to group assignment in this open trial"
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Quote: "Outcome measurement was not masked but used the automatic mode of the sphygmomanometer to measure blood pressure without the need for intervention by the investigator other than to place the cuff and switch the device on".
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Neither participants nor investigators were masked to group assignment
Incomplete outcome data (attrition bias) All outcomes	Low risk	15% loss to follow-up. Quote: "Similar results were recorded (for the primary outcome of systolic BP) where multiple imputation was used to replace missing values"
Selective reporting (reporting bias)	Low risk	The study protocol is available and outcomes are reported as specified apart from cost effectiveness and qualitative sub-studies which the authors state will be reported separately. Trial registered before recruitment (isrctn.com/ISRCTN83571366)
Other bias	Low risk	N/A

Morillo-Verdugo 2018

Study characteristics	
Methods	**Design:** 2-arm parallel RCT **Setting:** 5 tertiary hospitals in Spain **Duration of study:** 12 months (48 weeks)
Participants	**Number randomised:** 59; intervention: 26; control: 33. **Number lost to follow-up/withdrawn:** 6; intervention: 2 lost to follow-up; control: 3 lost to follow-up and 1 died from 'causes not related to the study'. **Number analysed:** 53 **Mean age in years (SD):** 53.6 (13.0); not provided by group assignment. **Age range:** Not reported **Gender (% women):** 9.4% **Proportion meeting criteria of 'primary prevention':** 100% (communication with study author) **Proportion prescribed medication for prevention of CVD:** lipid-modifying agents (28.0%), followed by drugs for acid-related disorders (10.0%), antithrombotic agents (9.0%), oral blood glucose–lowering drugs (8.0%), anxiolytics (6.0%), β-blockers (4.0%), antidepressants (4.0%), angiotensin converting enzyme inhibitors (4.0%), and drugs belonging to other therapeutic groups (27%) **Inclusion criteria:** people with HIV infection > 35 years of age; receiving active ART with at least 1 drug prescribed for the treatment of hypertension, dyslipidaemia, angina pectoris, cardiovascular prophylaxis, or type 2 diabetes; and at a moderate or high risk of CVD, as measured by the Framingham risk score **Exclusion criteria:** Patients who participated in clinical trials or who did not meet the inclusion criteria were excluded
Interventions	**Intervention:** Intensive pharmaceutical care was provided aimed at reducing cardiovascular risk. This consisted of pharmacotherapeutic follow-up (led by pharmacists) of all medication taken by the participant in order to detect and work toward the achievement of pharmacotherapeutic objectives related to cardiovascular risk and to make recommendations for improving diet, exercise, and smoking cessation. Participants were given information leaflets on cardiovascular risk prevention and an individual motivational interview to enhance this particular aspect. Participants were contacted periodically by sending text messages with content related to healthy living habits and health promotion **Comparison:** Participants included in the control group received the pharmacotherapeutic follow-up that was routinely applied to ambulatory care patients in the participating hospitals **How intervention was developed:** Not stated **Personalised intervention:** the non-mobile phone components were likely individualised given their nature, but report specifically states that text messages were not personalised **Frequency and duration of intervention receipt:** For the first 4 weeks, weekly messages were sent to the mobile phones of all participants who gave their informed consent, then periodically until the end of the follow-up period. Other components continued throughout 48 week follow-up period
Outcomes	**Primary outcomes:** Change in (continuous and proportion 'controlled'): Total cholesterol; LDL cholesterol; HDL cholesterol. Change in continuous diastolic blood pressure; systolic blood pressure; proportion 'controlled' blood pressure **Secondary outcomes:** Proportion adherent to 'concomitant medication' – note as above, this will included other medications not CVD-related (e.g. antidepressants) **Process outcomes:** None. **Adverse events:** Not reported. **Other outcomes (not for extraction):** BMI, triglycerides, alcohol intake, cigarettes, KIDMED score, physical activity, walking, ART adherence, Framingham risk score
Notes	**Funding source:** This project was awarded EUR 15,000 in the call for aid for working groups of the Spanish Society of Hospital Pharmacy (SEFH) in 2012 **Conflicts of interest:** The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article
Risk of bias	

Morillo-Verdugo 2018 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "assignment to the different groups was done through a sequence of random numbers, generated by specific software."
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "non-blinded study"
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Not described - outcomes extracted from medical records and interview during periodic dispensing of ART medication in the pharmacy service. BP measured by hospital pharmacist, and not clear if this was the same person delivering the intervention
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	self-reported outcomes - participants not blinded to group assignment
Incomplete outcome data (attrition bias) All outcomes	Low risk	6 out of 59 (~10%) participants lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No published study protocol, and no trial registry entry identified
Other bias	Low risk	N/A

Párraga-Martínez 2017

Study characteristics	
Methods	**Design:** 2-arm, parallel RCT **Setting:** primary care clinics in 3 health districts of 3 Spanish autonomous communities: Castile-La Mancha (Albacete), Aragon (Zaragoza) and Galicia (Vigo), Spain **Duration of study:** 24 months
Participants	**Number randomised:** 358; intervention group: 179; control group: 179 **Number lost to follow-up/withdrawn:** 54 (intervention group: 24 (reasons: 14 withdrew consent; 2 discontinued due to change of residence; 2 discontinued due to disease; 1 discontinued due to other reasons; 5 protocol violation); control group: 30 (reasons: 17 withdrew consent; 1 discontinued due to change of residence; 3 discontinued due to disease; 3 discontinued due to other reasons; 6 protocol violation) **Number analysed:** 304; intervention group: 155; control group: 149 **Mean age in years (SD):** intervention group: 58.9 (SD 10.4); control group: 59.3 (SD 8.4) **Age range:** not stated **Gender (% women):** intervention group: 56.1; control group: 53.7

Párraga-Martínez 2017 *(Continued)*

	Proportion meeting criteria of 'primary prevention': total: 93.1%; intervention group: 91.0%; control group: 95.3% **Proportion prescribed medication for prevention of CVD:** only statin use stated; total 68.1%; intervention group: 64.5%; control group: 71.8%). We contacted authors requesting trial data for those participants taking medication for primary prevention of CVD, but had no response **Inclusion criteria:** aged ≥ 18 years, previously diagnosed with defined hypercholesterolaemia (TC ≥ 250 mg/dL) who were receiving standard treatment (drug-based or not) and attending the participating centres **Exclusion criteria:** unable to undergo follow-up during the intervention (due to illiteracy or lack of a mobile telephone), had a physical disability impeding participation, or had a severe organic or psychiatric chronic disease precluding follow-up
Interventions	**Intervention:** participants received the following: written information on the disease and its treatment (provided at each visit); mobile telephone text messages with summaries of recommendations, reminders of dates of next appointments and notifications of new appointments if any previous ones were missed (during between-visit periods); and self-completed registration cards on adherence to recommendations (during the entire follow-up). Intervention group also received the standard recommendations of the European clinical practice guidelines for treatment of hypercholesterolaemia and cardiovascular risk. The intervention targeted lifestyle modifications, including healthy diet and physical activity, alongside medication adherence for those prescribed CVD medication **Comparison:** participants received the standard recommendations of the European clinical practice guidelines for treatment of hypercholesterolaemia and CVR **How intervention was developed:** not stated **Personalised intervention:** information provided not personalised, but reminders of dates of next appointment indicates some personalisation **Frequency and duration of intervention receipt:** the disease treatment reminders were sent every 15 days, whereas the attendance reminders for upcoming or missed appointments were sent according to the follow-up date. **Intervention duration:** 24 months (although not clear if this relates to all components of the intervention)
Outcomes	**Primary outcomes:** LDL-C; TC; HDL-C; SBP; DBP. All measured 2 years' post-randomisation. The medical outcomes are presented for entire sample, which includes participants not taking medication for primary prevention of CVD. We contacted authors requesting trial data for those participants taking medication for primary prevention of CVD, but had no response. Cardiovascular events in the observation period stated in protocol, but not reported in trial results **Secondary outcomes:** self-reported adherence to lipid-lowering therapy (measured using the Morisky-Green Test) at 2 years' post-randomisation **Process outcomes:** satisfaction with intervention (measured using a Likert scale satisfaction questionnaire) at 2 years' post-randomisation **Adverse events:** adverse effects of statins; intervention-related adverse effects
Notes	**Funding source:** funding from the Instituto de Salud Carlos III and the Health Research Project Subprogram of the European Regional Development Fund (PI12/01955), resolution 20 December 2012 **Conflicts of interest:** none declared

Risk of bias

Bias	Authors' judgement	Support for judgement

Párraga-Martínez 2017 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "participant randomization was centrally performed according to health care region (Efron randomization) by a researcher who was not involved in the interviews or analysis."
Allocation concealment (selection bias)	Unclear risk	Allocation of area was concealed; however, once areas were allocated, participants were allocated according to their area. It is not clear whether recruiting staff may have known to which area the participants belonged and therefore to which group they would be randomised
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants cannot be blinded due to nature of intervention, but report states "results were evaluated in a blinded manner."
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Not stated whether outcome measurements were taken by blinded personnel
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Participants cannot be blinded, and some outcomes were self-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Follow-up rate of 85% and no evidence of differential follow-up
Selective reporting (reporting bias)	Unclear risk	Outcomes reported as planned in protocol, with the exception of cardiovascular events occurring in the trial period which were stated in protocol but not included in trial report
Other bias	Low risk	N/A

Peiris 2019

Study characteristics	
Methods	**Design:** Stepped-wedge cluster RCT **Setting:** 54 villages served by 18 Primary Health Centres (PHC) in West Godavari District, Andhra Pradesh, India **Duration of study:** 24 months
Participants	**Number randomised:** 18 PHCs, 6 in each stepped-wedge group. 11,484 eligible participants at baseline. 15% randomly sampled at each of 4 time points. Total 8642; intervention period: 4348; control period: 4294 **Number lost to follow-up/withdrawn:** N/A – independent sample at each time point **Number analysed:** Total 8642; intervention period: 4348; control period: 4294 **Mean age in years (SD):** Intervention: 60.3 (10.71); control 61.0 (10.86) **Age range:** Note reported. **Gender (% women):** Intervention: 55.5%; control: 55.9% **Proportion meeting criteria of 'primary prevention':** Intervention: 82.6%; control: 83.5% **Proportion prescribed medication for prevention of CVD:** BP-lowering – Intervention: 41.8%; control: 42.3%. (Lipid-lowering – intervention: 4.2%; control: 3.7%. Anti-platelet – intervention: 2.7%; control: 2.4%) **Inclusion criteria:** PHCs were eligible if they were within 40 km from a major town, had at least 1 doctor regularly providing services, but with all doctors willing to participate in the study. Villages were eligible if most of its population accessed health care from their designated PHC, and the population of the village was not small (< 1900) or very large (> 10,000)

Peiris 2019 *(Continued)*

	Participants were eligible to participate if they were aged 40+, classified at high CVD risk and indicated for BP-lowering medication based on WHO and NPCDCS guidelines. High CVD risk and recommended for BP medication was defined as any of the following: 1) a past history of CVD; 2) an extreme BP elevation (SBP > 160 mmHg or DBP > 100 mmHg); 3) a 10-year CVD risk ≥ 30%; 4) a 10-year CVD risk of 20% - 29% and a SBP > 140 mmHg. CVD risk was estimated using algorithms based on the WHO/ISH risk charts tailored to the South-East Asian Region-D **Exclusion criteria:** Not able to provide informed consent
Interventions	**Intervention:** ASHAs and PHC doctors were trained to assess CVD risk using a clinical decision support system (CDSS) application on a tablet. The app allowed ASHAs to collect essential health-related information, inform the participant of their risk status, provide lifestyle advice relating to physical activity, diet and tobacco and alcohol and refer high-risk patients to the PHC doctor ASHAs conducted household-based assessments using the tablet. They measured BP and random capillary glucose samples. Data were uploaded to a shared electronic medical record (OpenMRS) in which 3 modules supported ASHAs to group patients who still required screening, prioritise workload, and alert them to high-risk individuals who required follow-up visits. Doctors accessed the data uploaded via OpenMRS and were provided with decision support recommendations for BP and other CVD risk factors management and medication prescription Participants received reminders on medication adherence and follow-up visits with the doctor via an interactive voice response system. This is an automated pre-recorded telephony service that notifies patients via a 1-way voice message of a particular action that was recommended to be taken. **Comparison:** During the control periods, participants in these PHCs/villages continued to receive their usual service provided by either a PHC doctor or a private doctor of their choosing. Any individuals identified at baseline to have extreme elevations of their BP were instructed to consult a doctor immediately **How intervention was developed:** protocol describes creation of the CDSS. No mention of the patient reminders **Personalised intervention:** No **Frequency and duration of intervention receipt:** Frequency unclear. Group 1 received the intervention for 18 months; group 2 for 12 months; group 3 for 6 months
Outcomes	**Primary outcomes:** Proportion achieving optimal blood pressure (systolic < 140 mmHg). Mean blood pressure. Self-reported new CVD events **Secondary outcomes:** Quality of life (EQ-5E) **Process outcomes:** Self-reported use of BP medicine **Adverse events:** None recorded **Other outcomes (not for extraction):** Other CVD risk factors (body mass index; current smoking; self-reported dietary intake and physical activity); self-reported use of BP and other cardiovascular medicines (from protocol)
Notes	**Funding source:** Australian National Health and Medical Research Council (NHMRC) Global Alliances for Chronic Disease Grant (ID1040147) **Conflicts of interest:** The authors have declared that no competing interests exist. The George Institute for Global Health has a wholly-owned social enterprise that is conducting commercial projects that include aspects of the intervention tested in this study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Cluster randomisation occurred at the level of the PHC. Central computer-based blinded randomisation was conducted with allocation stratified by population size"
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation of all 18 sites was conducted prior to commencement of the intervention at any PHCs."
Blinding of participants and personnel (performance bias)	High risk	Participants and PHC doctors could not be blinded to receipt of the intervention

Peiris 2019 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	An independent data collection team collected data at baseline and follow-up visits. They were blinded to the allocation of the village. Outcome analyses were conducted with the statisticians blinded to intervention allocation
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Unable to blind participants from the intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	15% random sample selected from control and intervention villages at each follow-up time. Whole cohort not followed
Selective reporting (reporting bias)	Low risk	The study protocol is available and outcomes are reported as specified. The only change is that CVD events were self-reported whereas the protocol states - 'hospitalisation data'. Trial registered before recruitment (CTRI/2013/06/003753)
Other bias	Low risk	Selective cluster recruitment Quote: "overall there were few (baseline) differences in the two samples"

Prabhakaran 2019

Study characteristics	
Methods	**Design:** 2-arms cluster RCT **Setting:** community health centres in 4 districts in Haryana (North India) and 2 districts in Karnataka (South India) **Duration of study:** 12 months
Participants	**Number randomised:** 3698 (40 clusters); intervention: 1842 (20 clusters); control: 1856 (20 clusters) **Number lost to follow-up/withdrawn:** 374 intervention: 205 (reason: 31 migrated; 84 refused; 56 unable to contact; 34 died); control: 169 (reason: 29 migrated; 86 refused; 33 unable to contact; 21 died) **Number analysed:** 3698, intervention: 1842; control: 1856 **Mean age in years (SD):** 55.1 (11.0); intervention: 55.8 (11.0); control: 54.5 (10.9) **Age range:** N/A **Gender (% women):** 44.8%; intervention: 42.7%; control: 46.9% **Proportion meeting criteria of 'primary prevention':** No previous CVD* at baseline: intervention: 95.6%; control: 91.3% * Previous ischemic heart disease, peripheral vascular disease, and stroke combined. **Proportion prescribed medication for prevention of CVD :** Not reported. But an author of the trial provided further information. Antihypertension drug: intervention 57.7%; control: 69.3%, lipid-lowering drug: intervention 5.1%; control 2.9% **Inclusion criteria:** ≥ 30 years of age, intended to reside in the catchment area of CHCs for ≥ 1 year, and had been diagnosed with hypertension with systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or type 2 diabetes mellitus with fasting blood glucose ≥ 140 mg/dL or postprandial blood glucose ≥ 200 mg/dL **Exclusion criteria:** Pregnant women, people with type 1 diabetes mellitus, patients requiring immediate referral to tertiary care because of accelerated hypertension or diabetic complications, people with learning difficulties or vision or hearing impairments, and people with malignancy or other life-threatening conditions

Prabhakaran 2019 *(Continued)*

Interventions	**Intervention:** In the intervention clusters, centralised training on the current clinical management guidelines was provided to all physicians, and training in the management of hypertension, diabetes mellitus, depression, and tobacco and alcohol use was given to NCD nurses. The NCD nurses used a tablet computer installed with the mWellcare system to collect data on patient history, blood pressure, blood glucose, depression, tobacco and alcohol use, and current medications. From this patient-specific clinical information, the mWellcare system generated a decision support recommendation (DSR) for the physician. Next, the physician referred the participant to the NCD nurse, who provided lifestyle advice using the prompts of the DSR, in addition to pamphlets (in the local language) to each participant. Additionally, through the mWellcare system, participants received short message service reminders for scheduled follow-up visits and medication adherence **Comparison:** Participants in control group received enhanced usual care. As in the intervention arm, the study provided training to physicians and NCD nurses on the clinical management guidelines for hypertension and diabetes mellitus; charts on the management of these conditions were displayed prominently at the outpatient clinics; and NCD nurses provided and explained the lifestyle advice pamphlet to each participant. In the control group, follow-up was at the discretion of the treating physicians **How intervention was developed :** developed by adapting existing clinical management guidelines to the local context, development, and validation of clinical algorithms and pilot-testing of the mWellcare system, which is an Android application designed to generate electronic decision support recommendations for the management of hypertension and diabetes mellitus, comorbid depression, and alcohol and tobacco use, tailored to the participant's profile and risk level. It stored the health records electronically, enabling long-term monitoring and follow-up. It was also equipped to send short message service reminders (to take medication and attend follow-up visits) to participants **Personalised intervention :** yes; information about scheduled follow-up visits and medication adherence sent via short message was personalised **Frequency and duration of intervention receipt:** 12 months
Outcomes	**Primary outcomes:** SBP, DBP, TC at 1 year from baseline **Secondary outcomes:** health-related quality of life (EQ-5D) but not reported in the trial paper; (only at the end of study) self-reported medication adherence during the last 7 days and participants' feedback on change in quality of care; costs but the results are not published **Process outcomes:** None reported **Adverse events:** protocol stated recording severe hypoglycaemia requiring medical attention/hospitalisation, CVD events, gangrene or amputation due to diabetes-related peripheral neuropathy and peripheral vascular disease, end-stage renal disease requiring renal replacement therapy, death, any other major health conditions/events **Other outcomes (not for extraction):** Glycated haemoglobin (HbA1c), fasting plasma glucose, BMI, tobacco use, alcohol use, predicted 10-year risk of CVD with the Framingham risk score recalibrated to the Indian population (only at the end of study) depression score diagnosed with the Patient Health Questionnaire-9
Notes	Clinicaltrial.gov, NCT02480062 **Funding source:** funded by the Wellcome Trust (grant 096735/A/11/Z) **Conflicts of interest:** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomisation list was generated by a statistician independent of the trial using STATA SE V. 12."
Allocation concealment (selection bias)	Low risk	This is a cluster-RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding of study participants or clinical personnel

Prabhakaran 2019 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Independent outcome assessors were hired Quote: "Given the nature of the cluster-randomized trial design, neither personnel nor participants were blinded to the intervention. Assessments at study end were carried out by independent outcome assessors"
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Participants were not blinded to the intervention. Adherence and perceived changes in quality of care were self-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "The sensitivity analysis performed by imputing missing values for outcome variables revealed similar results".
Selective reporting (reporting bias)	Unclear risk	Not all of the secondary outcomes have been reported; health-related quality of life and costs were not reported in the trial paper. Authors stated that the cost-effectiveness analysis would be conducted if the intervention showed a substantial effect. As it did not, there was no reason for them to present cost data. Supplementary materials list adverse events to be recorded, no mention of adverse events is made in trial report, although it is not clear whether this is because none occurred. Trial registered prior to recruitment (clinicaltrials.gov/ct2/show/NCT02480062)
Other bias	Unclear risk	Selective cluster recruitment - Quote: "the EUC arm had a higher proportion of participants with secondary education and above, employment, peripheral vascular disease, self-reported tobacco use and alcohol use, and higher mean SBP. Other baseline characteristics between the 2 arms were similar". Comment: This suggests SBP was different at baseline, but no statistical tests presented for these differences so could be due to chance

Saleh 2018

Study characteristics	
Methods	**Design:** 2-arm cluster RCT **Setting:** 16 primary healthcare centres located in rural areas and Palestinian refugee camps across Lebanon **Duration of study:** 12 months
Participants	**Number randomised:** Total: 2359; intervention: 1433; control: 926. 16 clusters in total, 8 in each arm. Hypertensive subgroup: intervention: 921; control: 626. **Number lost to follow-up/withdrawn:** Hypertensive subgroup, total: 257; intervention: 251; control: 6. (note all data collected from medical records) **Number analysed:** Hypertensive subgroup, total: 1290; intervention: 670; control: 620. **Mean age in years (SD):** Not reported. **Age range:** Not reported. Minimum age 40 years as per inclusion criteria. 42.6% of total sample in age range of 56 - 70 years **Gender (% women):** 56.2% **Proportion meeting criteria of 'primary prevention' :** Not reported **Proportion prescribed medication for prevention of CVD:** Not reported **Inclusion criteria:** registered at the primary healthcare centres (PHCCs) as diabetics or hypertensive and aged 40 years or more. Only Lebanese patients registered at the included Lebanese Ministry of Public Health (MOPH) PHCCs in rural areas and Palestinian refugee patients registered at the included

Saleh 2018 *(Continued)*

	United Nations Relief and Works Agency (UNRWA) health centres were eligible for inclusion if the aforementioned criteria were met **Exclusion criteria:** Records of patients whose nationality was not Lebanese nor Palestinian and whose age was less than 40 years were not eligible for inclusion
Interventions	**Intervention:** eSahha intervention consisted of 2 related components: 1 that is community-based and another that is PHC centre-based. The community-based component included community screening for HTN and diabetes among individuals falling within the age group at higher risk of developing NCDs —40 years or older—in the catchment areas of the 8 intervention centres. Individuals already diagnosed with or suspected of being diabetic, hypertensive, or both were referred to the nearest intervention PHCC for NCD-specific clinical care and were targeted by SMS messages. SMS content included health information on lifestyle, dietary habits, body weight, smoking, medications, importance of compliance, as well as symptoms and self-management of HTN and diabetes. Community individuals who were diagnosed and were receiving necessary care prior to the intervention were sent the weekly information SMS, as well as customised SMS reminders to follow up on their scheduled medical appointments. The PHC centre-based component of the intervention also included training of healthcare providers working in the intervention PHCCs, using (1) Online modules focusing on clinical guidelines for treating diabetes and HTN and others on provider-patient communication strategies (i.e. increasing compliance) and (2) Online forums and frequently-asked questions mainly dedicated to peer-to-peer knowledge-sharing of treatment and communication techniques **Comparison:** Individuals in the control group (i.e. living in catchment areas of control PHCCs) did not receive SMS messages and were thus receiving the usual care **How intervention was developed :** The SMSs were developed by a family physician based on the MOPH guidelines for prevention and management of HTN and diabetes **Personalised intervention:** The messages were initially formulated in English and then translated to Arabic and sent using simplified Arabic terms to match the different levels of health literacy of the target lay population. The PHC centre-based component of the intervention consisted of sending the same weekly informative health SMS, as well as appointment reminders customised to the respective time for check-ups to participants registered as diabetic or hypertensive at baseline at the PHCCs belonging to the intervention group **Frequency and duration of intervention receipt:** SMSs were sent once a week for a period of 1 year
Outcomes	**Primary outcomes:** Mean systolic blood pressure and diastolic blood pressure; proportion with 'controlled' blood pressure **Secondary outcomes:** None **Process outcomes:** None **Adverse events:** Not reported **Other outcomes (not for extraction):** Annual eye check-up. Among diabetes subgroup: Annual HbA1c testing; HbA1c poor control; HbA1c mean; proportion smokers; annual foot exam; exam eye check-up
Notes	**Funding source:** Not reported **Conflicts of interest:** None declared

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomly allocated" - no further information on how. Ensured 5 MOPH and 3 UNRWA centres in each group - so not completely random.
Allocation concealment (selection bias)	Low risk	cluster-randomised - included all eligible patients at each selected health centre
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding not possible - patients would know if they received SMS, and health centre staff would know if they were trained

Saleh 2018 *(Continued)*

Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	1 QI collector was hired at each of the 16 PHCCs included in the study (both intervention and control) to collect relevant QIs from patients' records at 2 points in time - unclear if blinded to what group PHCC was in
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	N/A
Incomplete outcome data (attrition bias) All outcomes	High risk	257 out of 921 in intervention group no outcome data; and only 6 out of 626 in control group. Discrepancy between groups not explained
Selective reporting (reporting bias)	Unclear risk	No published study protocol. Trial retrospectively registered (clinicaltrials.gov/ct2/show/NCT03580330)
Other bias	Low risk	Selective cluster recruitment - no statistical difference between the 2 groups except for age

Tobe 2019

Study characteristics	
Methods	**Design:** 2-arm parallel RCT **Setting:** First Nations populations living on reserve in 6 communities in Northern Ontario, Quebec and New Brunswick, Canada **Duration of study:** 12 months
Participants	**Number randomised:** 243 initially randomised. 101 excluded due to controlled BP during the 2-month baseline period. 142 received allocated intervention; 71 active intervention; 71 passive intervention **Number lost to follow-up/withdrawn:** 20; active intervention 7; passive intervention 13 **Number analysed:** 122; active intervention 64; passive intervention 58 **Mean age in years (SD):** active intervention 48.7 (12.8); passive intervention 49.1 (13.1) **Age range:** Not stated **Gender (% women):** active intervention 47.9%; passive intervention 50.7% **Proportion meeting criteria of 'primary prevention' :** Not stated – email from author (Tobe) says data not collected **Proportion prescribed medication for prevention of CVD :** Not stated in article. Email from author (Tobe): 28% on antihypertensives at baseline. **Inclusion criteria:** Aged 18+ years; living on reserve; uncontrolled hypertension (≥ 140/90 mmHg or ≥ 130/80 mmHg for diabetics); stable on current dose of antihypertensive (if treated) for at least 8 weeks; able to complete informed consent; have a mobile phone capable of receiving SMS text messages or be willing to carry and learn to use one for the study; have a current primary healthcare provider **Exclusion criteria:** Controlled BP on medication; BP > 180/110 mmHg; participation in other trials
Interventions	**Intervention:** Active and passive SMS text messages. 12 active messages explaining the importance of BP control and the rationale for medical therapy. They included information on the management of hypertension and advice to follow up with a healthcare provider if the measured BP was above target. 26 passive messages included healthy lifestyle and behaviour-change advice for diet. Individual BP measurements were taken by community health workers using an automated BP device with Bluetooth transmission capability to allow transmission of measurements to healthcare providers **Comparison:** Passive SMS text messages and individual BP measurements as above **How intervention was developed:** SMS text messages were derived from the Hypertension Canada Clinical Practice Guidelines by clinical researchers and modified with community input to make them culturally sensitive and specific. 1 focus group discussion was conducted in each of 3 Aboriginal communities. Participants were shown approximately 50 SMS messages and invited to discuss their interpretation of the content, including perceived positive and negative characteristics of the message.

Tobe 2019 *(Continued)*

	They also explored the acceptability, perceived control and motivation for the suggested behaviours (Maar 2016). **Personalised intervention:** Yes, participants were advised to see their healthcare provider if the measured BP was above target **Frequency and duration of intervention receipt:** Text messages were sent twice weekly to both groups throughout the study
Outcomes	**Primary outcomes:** Change in systolic and diastolic BP from the baseline period (first 2 months from randomisation) to the last 2 months of measurement. Proportion with controlled BP **Secondary outcomes:** N/A **Process outcomes:** Questionnaire assessment of knowledge gained from text messages (in protocol) **Adverse events:** Adverse events reported by each participant, deaths and hospitalisations **Other outcomes (not for extraction):** Pre-planned exploratory subgroup analyses by community, sex, diabetes status, phone ownership at baseline and age (in protocol)
Notes	**Funding source:** Canadian Institute of Health Research, Grand Challenges Canada, and International Development Research Centre **Conflicts of interest:** NRCCampbell (3rd author) is a paid consultant to the Novartis Foundation to support their program to improve hypertension control in low- to middle-income countries which includes travel support for site visits and a contract to develop a survey. NRCC has provided paid consultative advice on accurate BP assessment to Midway Corporation and is an unpaid member of World Action on Salt and Health

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomization to receive active and passive or passive only text messages took place at the time of enrolment by the central server software."
Allocation concealment (selection bias)	Low risk	Quote: "(randomisation) information was available only to the database manager; participants, clinicians, and study staff had no knowledge of randomization."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Participants were randomly allocated after enrolment….so that participants and study staff would not know which group participants had been enrolled", and the control received 'passive' messages containing general health education, meaning they would not have known which group they were in.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "study staff would not know which group participants had been enrolled", and blood pressure measurement throughout the study was performed by the CHR (Community Health Resource - a non-medical health worker) or local Home and Community Care nurses
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	14% loss. No information on these people
Selective reporting (reporting bias)	Low risk	Main outcomes reported but protocol mentions questionnaire to assess knowledge from text messages which is not mentioned in results paper. Trial registered April 2014 (clinicaltrials.gov/ct2/show/NCT02111226), prior to first recruitment which happened in February 2014
Other bias	Low risk	N/A

BMI: body mass index; BP: blood pressure; CVD: cardiovascular disease; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; ITT: intention to treat; LDL-C: low-density lipoprotein cholesterol; NIHR: National Institute for Health Research; RCT: randomised controlled trial; SBP: systolic blood pressure; SD: standard deviation; SMS: short messaging service; TC: total cholesterol.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Beratarrechea 2019	Follow-up < 12 months
Bosworth 2007	No mobile phone-specific intervention delivery
Bosworth 2018	No mobile phone-specific intervention delivery
Bove 2011	No mobile phone-specific intervention delivery
Broekhuizen 2010	No mobile phone-specific intervention delivery
Derose 2013	No mobile phone-specific intervention delivery
Ekinci 2017	Follow-up < 12 months
EMPOWER-SUSTAIN 2019	Follow-up < 12 months
Finkelstein 2009	No mobile phone-specific intervention delivery
Fischer 2014	No mobile phone-specific intervention delivery
Gerin 2007	No mobile phone-specific intervention delivery
Golshahi 2015	Follow-up < 12 months
Haramiova 2017	Follow-up < 12 months
Johnson 2000	No mobile phone-specific intervention delivery
Kessler 2018	Follow-up < 12 months
Kooy 2013	No mobile phone-specific intervention delivery
Margolis 2012	No mobile phone-specific intervention delivery
McGillicuddy 2015	Kidney transplant recipient population
McManus 2010	No mobile phone-specific intervention delivery
Meurer 2019	Follow-up < 12 months
NCT04066010	Follow-up < 12 months
Neafsey 2011	No mobile phone-specific intervention delivery
O'Connor 2014	No mobile phone-specific intervention delivery
Olorun 2014	Not a randomised controlled trial
Parati 2013	No mobile phone-specific intervention delivery

Study	Reason for exclusion
Richard 2016	No mobile phone-specific intervention delivery
Salisbury 2016	No mobile phone-specific intervention delivery
Ueda 2017	Follow-up < 12 months
Vollmer 2014	No mobile phone-specific intervention delivery
Wakefield 2011	No mobile phone-specific intervention delivery
Wald 2014	Follow-up < 12 months
Warren 2012	No mobile phone-specific intervention delivery
Wittig-Wells 2019	Follow-up < 12 months
Yatabe 2018	No mobile phone-specific intervention delivery
Zhechun 2018	Both arms received mobile phone component

Characteristics of studies awaiting classification *[ordered by study ID]*

ACTRN12614000956606

Methods	Design: 2-arm parallel RCT Setting: Hospital de Curacavi, Chile
Participants	Expected: 1054 Inclusion criteria: patients with an established diagnosis of diabetes mellitus type 2, with or without hypertension, registered at Curacavi Hospital, Chile, as of 15 June 2014 Exclusion criteria: none
Interventions	Intervention: SMS to reinforce participant attendance, helps participants adhere to medication and lifestyle changes, and alerts health personnel to inadequate adherence or changes in risk factors Control: standard care
Outcomes	Haemoglobin A1c, blood pressure, LDL cholesterol, urinary microalbumin, and participant adherence to appointments and medications (12 months)
Notes	

ACTRN12617001285347

Methods	Design: 2-arm parallel RCT Setting: Hospitals, New South Wales, Australia
Participants	Expected: 124

ACTRN12617001285347 *(Continued)*

	Inclusion criteria: diagnosed with at least 1 of the following chronic conditions: type 2 diabetes mellitus (T2DM), heart failure, hypertension (HT), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD); taking a minimum of 3 different medications; able to visit the clinic monthly over a 12-month period; iPhone accessibility; 18 to 70 years old Exclusion criteria: absence of a chronic disease controlled with medication; unable to correctly use the Perx app or an iPhone; inability to read and write English; participants may also be excluded, if in the opinion of the study Investigators, they have some other condition or disorder that may adversely affect the outcome of the study or the safety of the participant (e.g. psychiatric illness, substance abuse); unable to commit to the appointment schedule or perform the tasks required in the study
Interventions	Intervention: Participants randomised to the 'Perx' intervention group will be asked to download the Perx iPhone application (app). The participants will enter their personal and medication information (name, dose, timing) into the app under the supervision of their physician or research nurse. Users will begin to receive reminders each time their medication is due based on the information they entered initially. If they verify they have taken their medication at the scheduled time they will be eligible to receive an opportunity to win an intermittent reward through a gamified interaction. Users get rewarded with a game every time they verify that they have taken their medication at the right time. To verify medication adherence, the app requests the user to take a real-time, in-app photo of their medication within plus/minus an hour of when their medication is due. This photo cannot be taken from their existing gallery. The photos are saved on the Perx server and checked by Perx app designers Control: Standard care
Outcomes	Primary outcomes: Medication adherence through manual pill counts (number of pills prescribed vs number of pills taken will be compared) (12 months) Secondary outcomes: acceptability of Perx to participants; hospitalisation rates. Hospitalisation data will be collected by study medical officers in consultation with the participant or through access to patient medical records; pathological measures of cardiovascular disease. A venous blood sample will be collected and analysed for blood lipid levels; pathological measures of Type 2 Diabetes Mellitus. A venous blood sample will be collected and analysed for fasting blood glucose, HbA1c and lipid level; pathological measures of chronic kidney disease. A venous blood sample will be collected and analysed for blood microalbumin and serum creatinine; pathological measures of chronic obstructive pulmonary disease by performing lung function tests (all measured at 3, 6, 9, 12 months follow up)
Notes	

ChiCTR1800017829

Methods	Design: 2-arm parallel RCT Setting: hospitals, China
Participants	Expected: 394 Inclusion criteria: aged 18 to 75 years; systolic blood pressure ≥ 140 mmHg in the outpatient clinic; taking no more than 3 antihypertensive drugs Exclusion criteria: taking ≥ 4 kinds of antihypertensive drugs; systolic blood pressure ≥ 180/120 mmHg in the outpatient clinic; dialysis patients; patients with bilateral renal artery stenosis; patients receiving radiotherapy or chemotherapy; not using iOS or Android system intelligence mobile phone; current use of a smartphone medication adherence application; cannot provide a valid address
Interventions	Intervention: mobile application

ChiCTR1800017829 *(Continued)*

	Control: not clear
Outcomes	Primary outcomes: hypertension Secondary outcomes: Morisky 8-item medication adherence scale; GPAQ scale; SF-12 scale; diet self-report; consumer Health Activation Index
Notes	

ChiCTR1900026862

Methods	Design: 2-arm parallel RCT Setting: community hospitals, Shaanxi, China
Participants	Expected: 384 Inclusion criteria: adults (aged over 18 years); diagnosed with hypertension and currently using antihypertensive medications; BP < 220/120 mmHg at enrolment; with health records at studying CHCs. Participants also had to have a mobile phone capable of receiving texts or had access to a mobile phone and were able to read and complete informed consent Exclusion criteria: patients who had dementia, depression, serious heart, lung, and kidney diseases; were pregnant or in their lactation period
Interventions	Intervention: short message service and consultation Control: not stated
Outcomes	Primary outcomes: medication adherence; knowledge score; blood pressure Secondary outcomes: none stated
Notes	

ChiCTR2000030677

Methods	Design: 2-arm parallel RCT Setting: hospitals, Sichuan, China
Participants	Expected: 600 Inclusion criteria: aged between 18 - 80 years; with newly-diagnosed hypertension; or have a history of hypertension, with uncontrolled BP in the past 3 months (≥ 140/90 or ≥ 130/80 (if the participant has diabetes/renal disease)); able to use a smartphone. Exclusion criteria: secondary hypertension; heart failure; Hospitalised for acute myocardial infarction within 6 months; severe hepatic or renal disease (serum aspartate aminotransferase/alanine aminotransferase levels 3-times higher above the normal limit, or glomerular filtration rate (eGFR < 30 ml /min) or serum creatinine > 221umol/L); planning to do surgery within 6 months; history of malignant tumours; cognitive dysfunction or not able to take care of themselves; participating in other clinical trials
Interventions	Intervention: internet-based patient-primary care physician-cardiologist (PPC) integrated management model of hypertension

ChiCTR2000030677 *(Continued)*

	Control: usual care
Outcomes	Primary outcomes: systolic blood pressure Secondary outcomes: diastolic blood pressure; serum lipids; serum lipids; anti-hypertensive medication adherence; participant satisfaction; cost effectiveness; BP control rate
Notes	

ChiCTR2000034579

Methods	Design: 2-arm parallel RCT Setting: not stated
Participants	Expected: 200 Inclusion criteria: 1) Local registered population who are not expected to leave their current residence in the next year; 2) Aged 18 - 79 years; 3) Junior high school or above; 4) Able to use a smart phone; 5) Participants who sign the informed consent; 6) Population with high risk of cardiovascular metabolic diseases Exclusion criteria: 1) People with cardiovascular diseases (including stroke, coronary heart disease or myocardial infarction, severe cardiac insufficiency), cancer, diabetes, hypertension, dyslipidaemia, atherosclerosis, chronic obstructive pulmonary disease and pulmonary heart disease; 2) Secondary thyroid, hypothalamic pituitary, adrenal and other endocrine diseases; 3) Diseases requiring urgent treatment, such as acute infection, hypertensive crisis, diabetic ketoacidosis, etc.; 4) Severe liver and kidney dysfunction, autoimmune disease, or any serious fatal disease; 5) Those who have mental system disorders or are unable to co-operate due to various reasons (cognitive disabilities, obvious physical disorders.
Interventions	Intervention: Health education + mobile health interventions Control: Health education
Outcomes	Primary outcomes: Fasting serum glucose; insulin; TC; HDL-C; LDL-C; TG; creatine; urea; uric acid; hsCRP; HbA1c (12 months follow-up) Secondary outcomes: None stated
Notes	

ChiCTR-IOR-17013599

Methods	Design: 2-arm parallel RCT Setting: not stated
Participants	Expected: not stated Inclusion criteria: adult hypertensive people registered with primary health institutions; aged 30 years or older; had at least 2 primary care outpatient encounters in 12 months prior to screening with BP > 140/90 mmHg at the 2 most recent visits; smartphone-owners and ability to use mobile application Exclusion criteria: not stated

ChiCTR-IOR-17013599 *(Continued)*

Interventions	Intervention: home BP telemonitoring and social media with primary hypertension management Control: standard care
Outcomes	Primary outcomes: the proportion of participants with controlled BP; cardiovascular disease events Secondary outcomes: change in other cardiovascular disease risk factors; hypertension medication adherence
Notes	

ChiCTR-IOR-17014227

Methods	Design: 2-arm parallel RCT Setting: community health centre, Shaanxi, China
Participants	Expected: 105 Inclusion criteria: essential hypertension participants whose age is 18 and older; clinical diagnosis of essential hypertension: SBP ≥ 140 mmHg or DBP ≥ 90 mmHg, or both, by physicians and/or taking antihypertensive medication(s); have a smartphone which could access the Internet and install the application; able to read and communicate in Chinese Exclustion criteria: people with acute, terminal and psychiatric disease
Interventions	Intervention: mobile Application enhanced Nurse-led Intervention Control: standard care
Outcomes	Primary outcomes: blood pressure Secondary outcomes: BMI; waist circumference; hypertension self-care; quality of life (follow up not stated)
Notes	

CTRI/2017/09/009710

Methods	Design: 2-arm parallel RCT Setting: not reported
Participants	Expected: not reported Inclusion criteria: all individual greater ≥ 20 years of age; have metabolic syndrome; has a text message-capable mobile phone; knows how to receive IVRS audio messages; speak and read Hindi Exclusion criteria: not reported
Interventions	Intervention: mhealth Intervention - unidirectional daily IVRS audio clip will be used to deliver health messages and triggers to promote knowledge, healthy eating, exercise, self-efficacy, and medication adherence Control: standard care

CTRI/2017/09/009710 *(Continued)*

Outcomes	Primary outcomes: disease progression; knowledge about diabetes, hypertension, obesity, hypercholesteraemia Secondary outcomes: quality of life (EQ-5D questionnaire); cost effectiveness (12 months)
Notes	

CTRI/2018/10/015962

Methods	Design: 2-arm RCT Setting: rural areas of Udupi district, Karnataka (India)
Participants	Expected: 480 Inclusion criteria: the rural area in villages which are covered by ASHA workers has more than 13 elderly with co-morbid conditions of hypertension and diabetes mellitus as on the survey data report. Elderly in the age group of above 60 years in both gender who reside in selected rural areas of Udupi Taluk. Elderly who is on prescribed medications for selected chronic illness. Elderly and family caregiver who can speak and understand English or Kannada. Elderly with chronic illness or their care provider possess the mobile phone. Elderly with chronic illness who are willing to participate in this study. Elderly with chronic illness and of either gender aged above 60 years receiving long-term medications for more than 3 months Exclusion criteria: elderly who could not follow the instructions of the investigator. Elderly who are not diagnosed with any chronic illness and not on medications. Elderly with chronic illness who are newly-diagnosed and taking medication less than 3 months for their conditions. Elderly with chronic illness who had a previous experience of being part of any other project related to drug compliance. Elderly with any other major diagnosed co-morbid illness such as renal failure and other kidney disease, and other illness such as cancer in any situ, BPH, TB, HIV/AIDS
Interventions	Intervention: multicomponent behavioural intervention programme which includes medication education by using teach-back technique, drug card, information booklet, SMS to mobile phone Control: standard care
Outcomes	Primary outcomes: medication non-compliance of elderly with co-morbid chronic illnesses of hypertension and diabetes mellitus; improvement in medication compliance (Hill Bone Medication Adhrernce scores) Secondary outcomes: improvement in biophysiological values (blood sugar, HbA1, BP, lipid profile); increase in self-efficacy scores which will be measured by using MASES-R scale; increase in quality-of-life scores which will be measured by using WHO-QOL BREF Scale Client satisfaction; acceptability of the Multi-component Behavioral Intervention Programme (MBIP) by using rating scale (3, 6 and 12 months)
Notes	

DRKS00019022

Methods	Design: 2-arm parallel RCT Setting: medical centres, Germany
Participants	Expected: 2500

DRKS00019022 *(Continued)*

	Inclusion criteria: adult > 18 years; the presence of an NYHA class (II and III); a sufficient constellation of symptoms and risk factors (screening NYHA I) Exclusion criteria: insufficient cognitive skills to participate in the programme; expected low compliance; constellation of symptoms with contra-indication to exercise therapy; participation in other studies
Interventions	Intervention: app-based exercise training, monitoring and self-management Control: usual care
Outcomes	Primary outcomes: NYHA I: Participants in the IG have a 20% higher VO2max at 12 months after programme end compared to the KG; NYHA II/III: Participants in the IG are 30% less likely to be hospitalised for HF-related conditions in the 12 months after inclusion than participants in the KG. Secondary outcomes: improvement of the echocardiographic HF-related values; lower NT-proBNP values; improvement of vascular function in the FMD method; improvement of concomitant diseases; improving the quality of life; improvement of drug adherence
Notes	

ISRCTN10999269

Methods	Design: 2-arm cluster RCT Setting: 60 general practices in Anhui (China)
Participants	Expected: 3420 Inclusion criteria: aged ≥ 18 years; living in the selected villages for ≥ 6 months/year; diagnosed with hypertension Exclusion criteria: previous diagnosis of mental illness, serious illness, or disability
Interventions	Intervention: personalised hypertension management - support for self-monitoring, personalised daily message, supervised machine counselling, and signed quarterly feedback Control: usual care
Outcomes	Primary outcomes: systolic BP/diastolic BP measured using mercury sphygmomanometer at baseline and every 12 months after baseline for 5 years Secondary outcomes: quality of life; occurrence of hypertension-related complications (such as cerebral haemorrhage, coronary heart disease, myocardial infarction, cerebral infarction); healthcare utilisation; scores of objective behaviours
Notes	

ISRCTN15952379

Methods	Design: 2-arm parallel RCT Setting: GP practices, UK
Participants	Expected: 958 Inclusion criteria: willing and able to give informed consent for participation in the trial; aged ≥ 35 years; diagnosis of type 2 diabetes; taking oral glucose-lowering treatment, blood pressure-lower-

ISRCTN15952379 *(Continued)*

	ing treatment, or lipid-lowering treatment (diabetes treatments) either alone or in combination; has access to a UK-registered mobile phone and is able, if necessary, with help (e.g. relative, friend, neighbour), to send, understand and retrieve brief SMS text-messages in English; registered with a general practice participating in the trial Exclusion criteria: pregnant, has been pregnant in the last 3 months or planning pregnancy during the course of the trial; any other significant disease or disorder which, in the opinion of the investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial; insulin treatment without concomitant use of oral glucose-lowering treatment; admitted to hospital within the last 3 months for hyper- or hypoglycaemia (self-report); another person in the household already participates in this trial; currently using a pharmacist-managed monitored dosage system for supply of medication
Interventions	Intervention: text messaging system Control: usual care
Outcomes	Primary outcomes: composite cardiovascular outcome based on the UKPDS risk engine equations calculated using measures of glycated haemoglobin (HbA1c), systolic and diastolic blood pressure, high-density lipoproteins (HDL) cholesterol, and total cholesterol Secondary outcomes: long-term glycaemic control measured using HbA1c level in blood samples; systolic blood pressure measured using a sphygmomanometer; diastolic blood pressure measured using a sphygmomanometer; total and HDL cholesterol; quality-of-life measured using the EQ-5D-5L questionnaire
Notes	

ISRCTN82013652

Methods	Design: 2-arm parallel RCT Setting: Cambridge, UK
Participants	Expected: 542 Inclusion criteria: have a diagnosis of hypertension (high blood pressure); have been prescribed at least 1 antihypertensive (blood pressure lowering) medication; have a most recent blood pressure reading higher than 140/90 mmHg or gaps in collecting repeat prescriptions; can understand English and is able to provide informed consent; has a mobile phone and is familiar with sending and receiving text messages; the practice nurse or healthcare assistant is not aware of any other reason why the patient should be excluded Exclusion criteria: has a diagnosis of dementia or other cognitive difficulties that could affect study participation; has had a recent severe life-threatening event or are under treatment for another long-term health condition (e.g. cancer); take part in another medication adherence or digital intervention, or both
Interventions	Intervention: very brief intervention (VBI) facilitated by a practice nurse or healthcare assistant followed by a 12-month text-messaging programme or smartphone app Control: usual care.
Outcomes	Primary outcomes: blood pressure measured using A&D upper-arm blood pressure monitor Secondary outcomes: medication adherence measured by biochemical testing of the urine and by self-reports (i.e. 2 items from the MARS questionnaire and 2 additional single-item measures); full lipid profile and glucose levels for a subsample of participants, measured using blood samples; quality of life measured using EQ-5D-5L, and resource use using a self-reported questionnaire

ISRCTN82013652 *(Continued)*

Notes	

Jia 2020

Methods	Design: 2-arm cluster RCT Setting: primary care clinics, China
Participants	Expected: 19,008 Inclusion criteria: patients with diagnosed T2D and registered for receiving EPHS in the participating communities. Individuals are eligible for enrolment if they meet the following inclusion criteria: aged 18 – 75 years; residing in the community for the last 6 months with no plan of relocating; voluntary participation with informed consent Exclusion criteria: had severe physical or psychological problems; were unable to attend the site visit; unable to answer questions; were women in the process of, or planning for, pregnancy or breast-feeding; and those who have participated in any other clinical trials within the last 6 month.
Interventions	Intervention: participants receive at least 2 BG and 1 BP test, monthly, and lifestyle and treatment instruction from a 3-tiered contracted team. A mHealth platform, Graded ROADMAP, enabled test results uploading and sharing, and participant referral within the team. The intervention participants will be further divided into basic or intensive intervention group according to whether they were actively using the Your Doctor App Control: usual care
Outcomes	Primary outcomes: blood glucose control rate with glycated haemoglobin (HbA1c) Secondary outcomes: control rates and changes of ABC (HbA1c, BP and low-density lipoprotein cholesterol) and fasting BG, hypoglycaemia episodes and health-related quality of life (EuroQol (EQ-5D))
Notes	

JPRN-UMIN000025372

Methods	Design: 2-arm parallel RCT Setting: hospital, Tokyo, Japan
Participants	Expected: 450 Inclusion criteria: able to visit Tokyo Women's Medical University Hospital Department of Endocrinology and Hypertension for assessment; wish to try non-face-to-face medical communication and telemedicine; able to perform home blood-pressure measurements; age of 20 years or older at time of consent; those with essential hypertension Exclusion criteria: those who do not own a smartphone compatible with the telemedicine platform; past history of coronary diseases; those with diabetes mellitus, chronic kidney disease, history of stroke, or peripheral artery disease; those classified as Category III according to the cardiovascular risk chart by Japan Atherosclerosis Society; pregnant women and those with high possibility of becoming pregnant; secondary hypertension, excluding idiopathic hyperaldosteronism and primary aldosteronism after adrenalectomy; those judged by research administrator to be inappropriate for the study

JPRN-UMIN000025372 *(Continued)*

Interventions	Intervention: telemedicine group - after the initial assessment including a face-to-face interview, the participants will use network-attached sphygmomanometer to measure home blood pressure and consult physician by non-face-to-face communication to adjust antihypertensive treatment. Control: conventional therapy group will manually measure and record home blood pressure and visit clinics regularly to adjust antihypertensive treatment
Outcomes	Primary outcomes: home blood pressure Secondary outcomes: major adverse cardiovascular events (coronary events, hospitalisation for heart failure, stroke, doubling of serum creatinine); adverse events; vascular indices: Cardio-Ankle Vascular Index (CAVI), Augmentation Index (AI), Flow Mediated Dilation (FMD), Intima-Media Thickness (IMT), visceral fat area (DUALSCAN); laboratory data (blood and urine); questionnaires on quality of life and adherence (12 months)
Notes	

JPRN-UMIN000035898

Methods	Design: 2-arm parallel RCT Setting: Japan
Participants	Expected: 360 Inclusion criteria: hypertensive patients whose blood pressure at the clinic or physical check-up is more than 140/90 mmHg irrespective of taking antihypertensive agents Exclusion criteria: a person who cannot use smartphone application; diagnosed as secondary hypertension; has chronic atrial fibrillation; severe renal failure (eGFR < 15 mL/min/1.73m^2) or on dialysis; a history of major cardiovascular events within the past 3 months; antihypertensive medication was changed within the past 1 month; a plan of hospitalisation due to surgery or examination at the time of study participation; using another smartphone application for hypertension at the time of study participation; judged as inappropriate for the study participation by the principal investigator
Interventions	Intervention: Application Control: standard care
Outcomes	Primary outcomes: Change in systolic blood pressure from baseline Secondary outcomes: 1.Change in systolic blood pressure from baseline to 6 months; 2.Change in diastolic blood pressure from baseline to each follow-up point (6 months and 12 months); 3.Change in frequency of blood pressure measurements at home from baseline to each follow-up point (6 months and 12 months); 4.Quality of life (EQ-5D-5L); 5.Self-efficacy (GSES); 6.Medication-taking adherence (MMAS-4); 7.Medical cost; 8.Adverse events; 9.Change in number or dosage of antihypertensive medicine; 10.Days until change of antihypertensive medicine after the start of clinical study ; 11.Self-monitoring data; 12.Frequency of use of smartphone application
Notes	

JPRN-UMIN000038029

Methods	Design: 2-arm cluster RCT

JPRN-UMIN000038029 *(Continued)*

	Setting: Tanzania
Participants	Expected: 1600 Inclusion criteria: 18 to 70 years old; uncontrolled HT (SBP ≥ 140 mmHg and DBP ≥ 90 mmHg on at least 2 separate readings) or Type 2 DM (HbA1c > 7%); receiving care from participating health facilities; owns a mobile phone and has a voluntary family member who also owns a mobile phone Exclusion criteria: severely ill patients, any patient with complications related to HT and/or DM, type 1 DM, pregnant women, less than 18 years, and mentally ill
Interventions	Intervention: mHealth (text messaging) with support of community health promoters Control: standard care
Outcomes	Primary outcomes: HbA1c; systolic and diastolic blood pressure (6, 12, 24 months follow up) Secondary outcomes: adherence to medication; adherence to clinical visits (6, 12, 24 months follow-up)
Notes	

LoGerfo 2019

Methods	Design: 3 arm cluster RCT Setting: Cambodia
Participants	Expected: 4500 Inclusion criteria: all patients registered into the MoPoTsyo Patient Information Center system at the time of PE randomisation were included as the community sample to receive mHealth messages Exclusion criteria: none
Interventions	Intervention: Group 1 - providing electronic tablets to PEs for data collection and transfer to the MoPoTsyo database in Phnom Penh. The tablets are intended to speed up data collection and entry, reduce paper, increase accuracy, and eliminate lengthy distances that must be travelled to bring paperwork to MoPoTsyo. In addition, the tablets will allow PEs to scan a participant's record "handbook" (log kept with the participant) to be verified by MoPoTsyo quality-control staff should data appear suspicious. At the participant level, voice messages developed to address specific participant problems (e.g. uncontrolled blood pressure or glucose, medications not picked up at the pharmacy, weight gain, etc) will be sent to participants based on the data received from the monthly visits to the PE. Group 2 - tablet only Control: standard care
Outcomes	Control of blood pressure and glucose, medication adherence, use of medical services (laboratory and physician office visits), and improvement in lifestyle factors such as smoking, body mass index, diet, and exercise (12 months)
Notes	

Luong 2019

Methods	Design: 2-arm parallel RCT Setting: Veteran's Administration (VA) and the Denver Health and Hospital Authority (DHHA) healthcare systems, USA
Participants	Recruited: 400 Inclusion criteria: people with cardiovascular diseases and being treated with at least 1 medication Exclusion criteria: not stated
Interventions	Intervention: 'Nudge' text messages Control: not stated
Outcomes	Primary outcomes: not stated Secondary outcomes: not stated
Notes	

Meurer 2020

Methods	Design: factorial RCT Setting: Flint, Michigan, USA
Participants	Expected: 833 Inclusion criteria: age of 18 or greater; at least 1 BP with SBP ≥ 160 or a DBP ≥ 100 (criteria 1); if the patient has repeated measurements after achieving Criterion 1, at least 1 of the repeat BP remains SBP ≥ 140 or a DBP ≥ 90; just have cell phones with text-messaging capability and willingness to receive texts; likely to be discharged from the ED Exclusion criteria: unable to read English (< 1% at study site); prisoners; pregnant; pre-existing condition making 1-year follow-up unlikely; terminal illness with death expected within 90 days; current use of 3 or more antihypertensive agents; other serious medical conditions that prevent self-monitoring of BP; critical illness with placement in resuscitation bay; dementia/cognitive impairment
Interventions	Intervention arms: participants randomised into one of three component arms, consisting of varying intensity levels: (1) healthy behavior text messaging (daily vs. none), (2) blood pressure self-monitoring (daily vs. weekly), and (3) facilitated primary care provider appointment scheduling and transportation (yes vs. no).
Outcomes	Primary outcomes: change in systolic blood pressure Secondary outcomes: arrival at first primary care visit; attendance at primary care visits
Notes	

NCT03515083

Methods	Design: 2 arm parallel RCT Setting: USA
Participants	Expected: 100

NCT03515083 *(Continued)*

	Inclusion criteria: non-valvular atrial fibrillation that is either paroxysmal, persistent or permanent; CHA2DS2VASc score of 2 or more; eligible for therapy with apixaban for at least 6 months; possession of a smartphone capable of pairing with the AliveCor Kardia cardiac monitor Exclusion criteria: contraindication to anticoagulation with apixaban for at least 6 months; no access to a smartphone capable of pairing with the AliveCor Kardia cardiac monitor; unable to provide informed consent for this protocol
Interventions	Intervention: in the experimental group, each participant will be issued an AliveCor Kardia electrocardiogram monitor and application that is compatible with their smartphone. Participants will be instructed on the use of the monitor at the initial visit with the study nurse. The participant will submit daily electrocardiogram transmission via on online portal. The study nurse may contact them via text message to remind them to submit their recordings, if they forget Control: standard care
Outcomes	Primary outcomes: anticoagulation compliance Secondary outcomes: composite of deaths, strokes, and hospitalisations; AF symptom severity (12 months)
Notes	

NCT03515681

Methods	Design: 2-arm cluster RCT Setting: USA
Participants	Expected: 150 Inclusion criteria: > 3 systolic blood pressure measurements > 140/90 mmHg (2 in the previous 12 months + 1 at baseline); age 18 - 85 years; weight < 300 pounds; has a cell phone; can provide consent; speaks English or Spanish Exclusion criteria: none reported
Interventions	Intervention: text messages to promote seeking care and improving compliance with blood pressure treatment Control: messages about their kiosk blood pressure levels currently provided by higi to kiosk users. These messages are provided at the kiosk at the time of the blood pressure measurement (no text messages)
Outcomes	Primary outcomes: total number of participants with blood pressure control at 12 months Secondary outcomes: total number of participants with blood pressure control at 6 months; total number of participants with blood pressure control at 3 months; mean systolic pressure at 12 months; mean diastolic pressure at 12 months
Notes	

NCT03872856

Methods	Design: 2-arm cluster RCT

NCT03872856 *(Continued)*

	Setting: primary care centres, Alaska, USA
Participants	Expected: 324 Inclusion criteria: at least 1 visit to SCF providers or Community Health Aides within the previous year; Alaska Native or American Indian; at least 18 years old; Hypertension diagnosis based on International Classification of Disease (ICD) version 9 and/or ICD version10 codes; Systolic BP ≥ 130 mmHg recorded at 1 or more clinic visits in the past 18 months, OR systolic BP ≥ 130 mmHg at the study screening visit; ability to provide informed consent; Willingness and ability to use a a home blood pressure monitor (HBPM); willingness to complete the necessary data collection procedures, including transmission of BP measurements and permission for study staff to access EHR and/or PHR data Exclusion criteria: currently pregnant
Interventions	Intervention: participants in the BP-ICAN arm will receive a HBPM to be used twice daily for 12 months. Participants' home blood pressure measurements will be shared with their provider and participants will receive a series of text messages including topics on the importance of managing hypertension, reminders to measure blood pressure with their device, and motivational messages on diet and exercise Control: standard care
Outcomes	Primary outcomes: individual-level: within-person change in systolic blood pressure (Time frame: 12 months) Secondary outcomes: provider-level: frequency of antihypertensive medication adjustments (Time frame: 3 months, 6 months, and 12 months); system-level: change in systolic blood pressure for all participants with hypertension (Time frame: 12 months)
Notes	

NCT03986931

Methods	Design: 2-arm parallel RCT Setting: Family Medicine, River Crossings, Scott Blvd, or Muscatine University of Iowa Clinics, USA
Participants	Expected: 420 Inclusion criteria: fluent in English or Spanish; Have a clinic-measured blood pressure of ≥ 145 mmHg and/or ≥ 95 mmHg at 2 previous clinic visits or 1 previous clinic visit and on the day of enrolment; must be a patient at Family Medicine, River Crossings, Scott Blvd, or Muscatine University of Iowa Clinics; live in a zip code that is scored as a 4 - 10 on the Rural-Urban Commuting Area codes Exclusion criteria: currently pregnant or planning to become pregnant in the next year; upper-arm circumference > 50 cm (20 in); prisoner status; unable to provide own informed consent
Interventions	Intervention: participants enrolled in the Pharmacist-Bidirectional Texting Group will return 7 morning and 7 evening blood- pressure measurements via text message. The report will be shared with a pharmacist who will monitor them for 12 months. The pharmacist will have access to their entire medical record and will provide support and education via text messaging, email, or phone calls, whichever is preferred by the participant. The pharmacist will develop a care plan and make recommendations to the physician through the electronic medical record to quickly adjust therapy to improve control. They will also recommend laboratory testing if indicated. They will have contact with the participant every 2 - 3 weeks while blood pressure is uncontrolled, and at least every 2 months when it is controlled. The pharmacist will track all recommendations made to physicians and whether or not they were implemented, modified, or rejected

NCT03986931 *(Continued)*

	Control: participants randomised to the control group will also return 7 morning and 7 evening blood-pressure measurements. The report will be shared with a pharmacist who will call the participant to discuss the measurements and possibly recommend follow-up with a physician, but no other pharmacist intervention or monitoring will occur
Outcomes	Primary outcomes: change in systolic blood pressure Secondary outcomes: change in diastolic blood pressure; number of medication changes; cost (12 months)
Notes	

NCT04076020

Methods	Design: 2-arm parallel RCT Setting: Western Pennsylvania, USA
Participants	Expected: 264 Inclusion criteria: Adult, age ≥ 18; Diagnosis of AF, identified from the EHR problem list and confirmed by 2 or more reports of AF from separate monitoring events at least 2 weeks apart (CG, Holter or event monitor); CHA2DS2-VASc (heart failure, hypertension, age, diabetes, prior stroke/TIA, CD, female sex) ≥ 2; Prescribed use of warfarin or DOAC (formerly NOAC) for AF stroke prevention; English-speaking well enough to participate in informed consent and this study; No plans to relocate from the area within 12 months of enrolment Exclusion criteria: Conditions other than AF that require anticoagulation, such as mechanical prosthetic valve, deep vein thrombosis, or pulmonary embolism; History of pulmonary vein isolation or foreseen pulmonary vein isolation; History of AV nodal ablation or foreseen AV nodal ablation; Heart failure necessitating hospital admission ≤ 3 months prior to study inclusion; Acute coronary syndrome (defined as at least 2 of the following: chest pain, ischaemic electrocardiographic changes, or troponin ≥ 0.1 ng/mL) ≤ 3 months prior to study inclusion; Untreated hyperthyroidism or ≤ 3 months euthyroidism before inclusion; Foreseen pacemaker, internal cardioverter defibrillator, or cardiac resynchronisation therapy; Cardiac surgery ≤ 3 months before inclusion; Planned cardiac surgery; Presence of non-cardiovascular conditions likely to be fatal within 12 months (e.g. cancer); Inability to comprehend the study protocol, defined as failing to answer correctly a set of questions on orientation and short-term memory during the consent process
Interventions	Intervention: smartphone-based intervention called an embodied conversational agent (ECA) which simulates conversation and provides coaching, guidance, and assistance with chronic disease self-management. In addition participants will receive an AliveCor Kardia for heart rate and rhythm monitoring, an FDA-approved, widely-used instrument that pairs with the relational agent Control: participants will receive a smartphone as well, which will have the health application WebMD
Outcomes	Primary outcomes: Medication possession ratio (12 months) Secondary outcomes: Self-reported adherence; Change from baseline Atrial Fibrillation Effect on QualiTy of life (AFEQT); Emergency room visits; Urgent care visits; Days of hospitalisation (4, 8, 12 months)
Notes	

NCT04259489

Methods	Design: 2-arm parallel RCT Setting: China
Participants	Expected: 210 Inclusion criteria: 18 - 80 years old diagnosed with type 2 diabetes; signed Informed consent form content; can be regularly followed (every 3 months) for at least 1 year Exclusion criteria: important organ failure or other severe diseases including infection, mental disorder, heart failure or disseminated intravascular coagulation; active or inactive malignant tumour, expectation of life less than 1 year; communication disorders, cannot communicate and/or co-operate; women who are pregnant, breast-feeding, or conception plan in the recent year
Interventions	Intervention: Shared Care model: pay regularly quarterly visit to a multidisciplinary team led by physician at outpatient clinic, and receive remote and systematic management and education online after going home Control: usual care
Outcomes	Primary outcomes: Glycemic achieving rate Secondary outcomes: HbA1c change; blood pressure change and rate of reaching the standard; LDL-c changes and rate of reaching the standard; Morisky scale score change (1 year follow-up)
Notes	

NCT04409210

Methods	Design: 2-arm parallel RCT Setting: not stated
Participants	Expected: 8840 Inclusion criteria: participants - aged ≥ 18 years; meet any of the following indicators: 1) LDL-C > 4.9 mmol/L or TC > 7.2 mmol/L; 2) Diabetic patients (age > 40 years old): 1.8 mmol/L ≤ LDL-C < 4.9 mmol/L (or) 3.1 mmol/L ≤ TC < 7.2 mmol/L; 3) The predicted risks measured by China-PAR model of ≥ 10%; 4) Patients with predicted risks measured by China-PAR model of ≥ 5% and < 10%, and meet with 2 or more risk factors as following: Systolic Blood Pressure ≥ 160 mmHg or Diastolic Blood Pressure ≥ 100 mmHg, BMI ≥ 28 kg/m^2, Non- HDL-C ≥ 5.2 mmol/L, Smoking, HDL-C < 1.0 mmol/L. (3) Local permanent residents (more than 5 years); (4) No severe physical disability, clear consciousness and normal communication; (5) The participants in the intervention group or their families have smartphones; (6) Disease and death are under the management of the local health department; (7) Sign the informed consent form voluntarily Family physician teams - the number of residents served is more than 30,000; the proportion of high-risk population of cardio-cerebrovascular diseases is more than 8%; manage the health records of residents; have a health examination for the residents once a year; family doctors have smartphones Exclusion criteria: patients: temporary residents and floating population; those who have serious health conditions and are unable to participate in this study; those who are unwilling to accept the follow-up inspection; according to the judgement of the researchers, are not suitable to participate. Family physician teams - the establishment of residents' health records is incomplete; the main population served are temporary residents and floating population

NCT04409210 *(Continued)*

Interventions	Intervention: smartphone App Control: usual care
Outcomes	Primary outcomes: rate of atherosclerotic cardio-cerebrovascular events Secondary outcomes: number of newly-acquired high-risk factors of cardiovascular and cerebrovascular diseases; number of participants with major adverse cardiovascular events; health-related quality of life; medication adherence; number of participants with new-onset atrial fibrillation or atrial flutter; number of participants with peripheral artery disease; consumption of medical resources (3 years follow-up)
Notes	

PACTR201811878799717

Methods	Design: 2-arm parallel RCT Setting: South Africa
Participants	Expected: 1500 Inclusion criteria: diagnosed with HIV and Hypertension; on ART and on blood pressure-lowering medication (or about to start); BP at recruitment > 140/90 mmHg; within 8 weeks of a viral load test (to offset the cost of baseline viral load and reduce the overall cost of the study); accessing care for both HIV and hypertension at selected sites; have regular access to a mobile phone and able to access SMS text messages; > 18 years of age and willing to participate and give written informed consent Exclusion criteria: requiring specialist care for hypertension; self-reported pregnancy or within 3 months post-partum; very high BP (systolic > 220 mmHg or diastolic > 120 mmHg) or symptoms suggestive of hypertensive emergency; active malignancy or ongoing treatment for malignancy; acutely unwell patients
Interventions	Intervention: text messages to motivate collecting and taking medicine and to provide education about and motivation for secondary adherence, in particular, on healthy lifestyle choices (nutrition, physical activity, stress management). Additional reminders will be sent when medicine are ready for collection or about scheduled clinic appointment Control: a welcome message, a message confirming enrolment and other SMS text-messages about participation in the trial. Delivery of SMS text-messages will be automatically tracked and if undelivered, a research assistant, blinded to group allocation, would contact the number of a friend or relative to obtain a new mobile phone number
Outcomes	Primary outcomes: mean difference in systolic and diastolic blood pressure Secondary outcomes: 1) uptake and adherence to BP medications, 2) uptake an adherence to HIV specific medications, 3) mean change in lipid variables, 4) mean change in CD4 count and viral load, 4) mean change in adiposity variables, 5) change in kidney function Tertiary - 1) Descriptive analysis of the process involved in the intervention, 2) Economic analysis, 3) Quality of life (12 months)
Notes	

Polgreen 2020

Methods	Design: 2-arm parallel RCT Setting: not stated
Participants	Expected: not stated Inclusion criteria: not stated Exclusion criteria: not stated
Interventions	Intervention: bi-directional texting platform for home BP measurements that can then be managed by clinical pharmacists located remotely Control: not stated
Outcomes	Primary outcomes: mean systolic blood pressure (12 months follow-up) Secondary outcomes: diastolic BP, number of medication changes and costs
Notes	

Ramallo-Fariña 2020

Methods	Design: 4-arm cluster RCT Setting: Canary Islands
Participants	Recruited: 2334 Inclusion criteria: Patients - T2DM diagnosis; aged between 18 and 65; health professionals - primary healthcare teams (PHCT) comprising a primary care physician and a nurse practitioner associated to a patient will be selected; must have a permanent position or a stable substitute position Exclusion criteria: peripheral vascular disease; diabetic nephropathy and/or chronic kidney disease; cognitive impairment, dementia; major depression; insufficient level of Spanish; pregnant or planning to become pregnant in the next 6 months; cancer last 5 years; ischaemic disease or heart failure; proliferative diabetic retinopathy
Interventions	Intervention: educational group programme and monitored and supported by logs, a web-based platform, and automated SMS; intervention for professionals also received an educational programme, a decision support tool embedded in the electronic clinical record, and periodic feedback about participants' results Control: usual care
Outcomes	Primary outcomes: change in glycosylated haemoglobin (HbA1c) Secondary outcomes: change in total cholesterol level; change in HDL level; change in LDL level; change in triglycerides; change in EQ-5D index; change in Morisky Compliance Scale
Notes	

Schmidt 2018

Methods	Design: 2-arm parallel RCT

Schmidt 2018 *(Continued)*

	Setting: University Medical Center Rostock (UMR) or Helios Klinik Schwerin (Schwerin). In addition, inpatients of the UMR or Helios Klinik Schwerin, Germany
Participants	Expected: 964 Inclusion criteria: heart failure (I50, NYHA II - IV) or atrial fibrillation (I48, EHRA II - IV) or resistant hypertension (I 10 - 15, ≥ 3 antihypertensive medicines from different drug classes, SBP > 140 / 90mmHg or ≥ 4 antihypertensives irrespective of the blood pressure, with at least 1 drug being a diuretic); member of health insurance company AOK Nordost or Techniker Krankenkasse (TK); inscription to integrated care contract with the health insurance company; residence in Mecklenburg-Vorpommern; age ≥ 18 years; written informed consent Exclusion criteria: pregnancy, suspected pregnancy or breast-feeding period; participation in another clinical trial up to 30 days before inclusion in this trial; cognitive deficits: participants need to be able to read and understand German language as presented on a tablet; chronic kidney disease requiring dialysis or creatinine clearance < 15 ml/min
Interventions	Intervention: the care centre is at the heart of the NICC structure. It will be available 24/7. It is the core platform to share information for all NICC patients in the care process and serves as integration point between the professional groups. The care centre is using the NICC platform for care coordination and patient monitoring. The NICC platform enables patient management from the distance and allows treating physicians to observe and follow the health status of patients daily. Using the NICC tablet, participants provide information from home about their health status. They will receive feedback about their therapy, measurements and reminders and motivation to follow care plans. The communication allows for a regular evaluation of the participant's situation, a review of the therapy and co-ordination of necessary adjustments with care providers. The general intervention rules are based on the current European Society of Cardiology (ESC) guidelines for treating AF, HF and TRH patients Control: standard care
Outcomes	Primary outcomes: composite endpoint death and cardiovascular events; hospitalisation; composite endpoint death and broader cardiovascular events. Secondary outcomes: adherence to novel integrated care concept; quality of life; cost; safety; beliefs about medication questionnaire; time-to-event; medication adherence; Illness-specific Social Support Scale Short version-8; patient activation measure; heart-specific quality of life; patient health questionnaire depression module; generalised anxiety disorder scale; WHO well-being index
Notes	

Steinert 2020

Methods	Design: not stated Setting: not stated
Participants	Recruited: 100 Inclusion criteria: not stated Exclusion criteria: not stated
Interventions	Intervention: smartphone application over 12 months - users of this app could set reminders to keep track of their medication and other disease-related variables, such as weight and cholesterol Control: not stated
Outcomes	Primary outcomes: not stated

Steinert 2020 *(Continued)*

	Secondary outcomes: not stated
Notes	

Tahkola 2020

Methods	Design: 2-arm parallel RCT Setting: primary care, Finland
Participants	Recruited: 111 Inclusion criteria: a clinical diagnosis of hypertension; about to start medication for hypertension for the first time; aged 30 - 75 years; must own a mobile phone; must be able to read text messages; must be able to master own medication; must be able to perform home BP measurements; must agree to using electric drug prescription (standard in Finnish health care) Exclusion criteria: having or is suspected to have depression or psychosis; serious disease, which is evaluated to have an impact on life expectancy; atrial flutter or atrial fibrillation; previous history of antihypertensive medication; pregnancy; not willing to give informed consent and take part in the study; systolic BP more than 200 mmHg; diastolic BP more than 120 mmHg; sudden onset or worsening of hypertension; clinical signs of kidney disease: proteinuria (du-prot > 500 mg), glomerulus filtration rate (eGFR) less than 45 ml/min or hypokalaemia
Interventions	Intervention: personalised text message support and a checklist for initiation of antihypertensive medication Control: usual care
Outcomes	Primary outcomes: the proportion of participants achieving the systolic blood pressure target Secondary outcomes: measured medication adherence; change in systolic and diastolic blood pressure; hypertension-related use of healthcare services; perceived quality of life; proportion of participants knowing the adequate home BP; the proportion of participants whose BP target is adequately set; the quality and quantity of self-monitored blood pressure; ECG; blood glucose level; blood cholesterol level; microalbuminuria; creatinine level; body mass index; waist circumference; exercising habits; smoking; alcohol use
Notes	

Tekkesin 2018

Methods	Design: 2-arm parallel RCT Setting: not reported
Participants	Expected: not reported Inclusion criteria: patients between 20 to 79 years old who are at high risk for CVD (10 years ASCVD risk 7.5%) Exclusion criteria: patients with prior CVD events are excluded from the study
Interventions	Intervention: mobile technology plus usual-care group will receive a group of smart devices including mobile phone, wristband, weight scale and blood pressure monitor

Tekkesin 2018 *(Continued)*

	Control: standard care
Outcomes	Primary outcomes: change in ASCVD risk score Secondary outcomes: risk factor management (resting blood pressure, fasting glucose and HbA1C, fasting lipid levels, weight and BMI, smoking status, physical fitness); improvement in surrogate markers of atherosclerosis (hs-CRP and CIMT); quality of life; change in VO2 by CPET; major adverse cardiovascular events (death, MI, Stroke, cardiovascular hospitalisation)
Notes	

Ueda 2020

Methods	Design: 3-arm parallel RCT Setting: not stated
Participants	Recruited: 92 Inclusion criteria: not stated Exclusion criteria: not stated
Interventions	Intervention: interactive mobile phone support and to follow health service of diet, salt and antihypertensive treatment for 4 years in hypertension Control: standard care
Outcomes	Primary outcomes: blood pressure Secondary outcomes: not stated
Notes	

Williams 2020

Methods	Design: stepped-wedge cluster-randomised trial Setting: not stated
Participants	Expected: not stated Inclusion criteria: not stated Exclusion criteria: not stated
Interventions	Intervention: participant coaching, automated texting, peer phone support, academic detailing and audit and feedback for the participant's clinician Control: not stated
Outcomes	Primary outcomes: change in ASCVD risk Secondary outcomes: not stated
Notes	

Characteristics of ongoing studies *[ordered by study ID]*

AF-EduApp 2018

Study name	Effect of targeted education for atrial fibrillation patients (application substudy) (AF-EduApp)
Methods	**Design:** 4-arm parallel RCT **Setting:** Antwerp, Belgium: Antwerp University Hospital, Jessa Hospital
Participants	**Expected:** 221 **Inclusion criteria:** Over 18 years; patients in whom AF or atrial flutter is diagnosed with an electrocardiogram (12-lead, holter,...); patients who are capable to sign the informed consent **Exclusion criteria:** Not able to speak and read Dutch; cognitive impaired (e.g. severe dementia); life expectancy is estimated to be less than 1 year; ongoing participation in another clinical trial; pregnant women
Interventions	**Intervention:** Group 1: Application-driven education (AF-EduAppsubstudy)- Education will be given via a newly-developed application. Medication adherence (oral anticoagulation) will be measured using a special bottle cap that fits on a medication bottle. The participants in this group will receive feedback (notification or alarm, or both) during the entire study period via this application when they have to take their medication. Group 2: In-person education (AF-EduCare study)- Education will be given on regular basis via predefined consultation visits. Medication adherence (oral anticoagulation) will also be measured using a special bottle cap that fits on a medication bottle. If adherence is low, the participant will get additional feedback when he does not take this medication as prescribed Group 3: Online education (AF-EduCare study) Education will be given on regular basis via a special designed online platform. Medication adherence (oral anticoagulation) will also be measured using a special bottle cap that fits on a medication bottle. If adherence is low, the participant will get additional feedback when he does not take this medication as prescribed **Control:** Standard care
Outcomes	**Primary outcome:** Participants' adherence to medication (oral anticoagulation), measured by the Medication Events Monitoring System (MEMS). (Time frame: Monitored between 0 - 12 months and 12 - 15 months if resources allow) **Secondary outcomes**: Patrticipats' knowledge level, assessed by the Jessa Atrial fibrillation Knowledge Questionnaire (JAKQ) (Time frame: at baseline,1 month,3-,6-,12 months in the application group); Participants' quality of life, assessed by the EQ-5D-3L questionnaire and the Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) Questionnaire; participants' symptom burden, assessed by the Leuven ARrhythmia Questionnaire (LARQ); participants' self-care capabilities, assessed by the Self-Care Questionnaire (SCQ).(Time frame: at baseline,3-,6-,12 months in the application group. In the standard care groups at baseline and 12 or 18 months) participants' satisfaction with the intervention will be assessed by a study-specific Patient Reported Outcome Measure (PROM) questionnaire. (Time frame: at 12 months in all intervention groups and 12 or 18 months in the standard care groups)
Starting date	October 2019
Contact information	Michiel Delesie michiel.delesie@uza.be
Notes	ClinicalTrials.gov NCT03788044

BETTER-BP 2020

Study name	Behavioral Economics Trial To Enhance Regulation of Blood Pressure (BETTER-BP)
Methods	**Design:** 2-arm parallel RCT **Setting:** New York City, USA - participants recruited from 3 New York City Health and Hospital ambulatory clinics
Participants	**Expected:** 435 **Inclusion criteria:** 18 years or older; diagnosis of hypertension; Active prescription of 1 or more antihypertensive medication; SBP ≥ 140 mmHg (on therapy); suboptimal adherence **Exclusion criteria:** Incarcerated; pregnant; unable to study software in English or Spanish; unwilling/unable to consent; clear barrier to technology use (visual or hearing impaired), projected life expectancy under 12 months
Interventions	**Intervention:** Delivered by the Way to Health platform, installed on a smartphone and communicates with participants via text message. Participants are eligible to receive a potential cash reward if they are adherent with their antihypertensive medication the day before, which is monitored via electronic monitoring device (EMD) from AdhereTech. Each participant is assigned a 2-digit number for the trial, and each day the Way to Health platform randomly generates a 2-digit number. Participants will receive a prize if both digits match (1 in 100 chance) and will receive a prize of lesser value if one digit matches (18 in 100 chance). If they are not adherent with their medication, but would have won if they were adherent, they receive a text message that they would have won ("regret" component). This happens for 6 months **Control:** 3 in-person study visits, approximately 1 hour each. These will take place at baseline, 6 months, and 12 months
Outcomes	**Primary outcome:** Change in SBP (time frame: 12 months); Adherence to medication (timeframe: 12 months) **Secondary outcomes:** Motivation measured with the Treatment Self-Regulation Questionnaire (TSRQ) (Time frame: Baseline, 6 months, and 12 months); self-efficacy measured by the Medication Adherence Self Efficacy Scale (MASES) (time frame: 12 months); Comorbidity burden will be evaluated (baseline) using the Charlson Comorbidity Index (CCI) (Time frame: Baseline; Depression will be measured (baseline) by the PHQ-9 (Time frame: 12 Months); Patient-reported health status will be measured (baseline) using the Short Form 12 (SF-12). (Time frame: 12 months)
Starting date	July 2020
Contact information	Lysy Gonzalez lysy.gonzalez@nyulangone.org
Notes	ClinicalTrials.gov NCT0411466

Buis 2019

Study name	Improving blood pressure among African Americans with hypertension using a mobile health approach (the MI-BP App): protocol for a randomized controlled trial
Methods	**Design**: 2-arm, parallel RCT **Setting**: Detroit Medical Center (DMC) in the Emergency Departments of Detroit Receiving Hospital (DRH) and Sinai-Grace Hospital (SGH), both located in Detroit, Michigan, USA
Participants	**Expected:** 396

Buis 2019 *(Continued)*

	Inclusion criteria: aged 25 - 70 years; of African-American descent; have a previous diagnosis of hypertension; have uncontrolled BP (SBP > 135 mmHg) at triage and on repeat medication; have a smartphone compatible with the mobile intervention **Exclusion criteria:** pregnant; serious existing medical conditions which make BP control difficult or need frequent hospitalisation (i.e. resistant HTN, steroid-dependent asthma or emphysema, cirrhosis, hepatic failure, stage C or D chronic heart failure, stage IV or V coronary artery disease, terminal cancer or ongoing radiotherapy or chemotherapy); history of other serious medical condition (i.e. stroke, dementia, myocardial infarction or coronary artery disease); history of alcohol or drug abuse determined by CAGE score of over 2
Interventions	**Intervention:** Patients are assessed and undergo medical titration for optimal hypertension control; this is repeated in weeks 8, 13, 26, 39 and 52 of follow-up. This assessment looks at BP, health status, weight, adherence to BP measurements, physical activity, sodium intake and medication adherence and compares to data from the MI-BP app. At weeks 0, 26 and 52 renal and metabolic issues were also monitored, and a 24-hour urine collection is taken to analyse sodium intake. Study participants are given access to the MI-BP app for 12 months which includes at-home BP measuring, physical activity monitoring, sodium intake monitoring, goal setting and messaging services to aid hypertension monitoring **Control:** Enhanced usual care: prescription antihypertensive medications, printed educational materials on HTN and a home BP monitor for daily use. Control participants are also followed up at weeks 8, 13, 26, 39 and 52
Outcomes	**Primary outcome:** Difference in mean change in SBP (from baseline to 1 year) after using the MI-BP app; Cost effectiveness of MI- BP compared to usual care **Secondary outcome:** Mean improvements in physical activity, BP, sodium intake, and medication adherence due to use of the MI BP app
Starting date	January 2018
Contact information	Lorraine R Buis: buisl@umich.edu
Notes	ClinicalTrials.gov NCT02360293; clinicaltrials.gov/ct2/show/NCT02360293

Byrne 2018

Study name	The Ready to Reduce Risk (3R) Study for a group educational intervention with telephone and text messaging support to improve medication adherence for the primary prevention of cardiovascular disease: protocol for a randomized controlled trial
Methods	**Design:** 2-arm, parallel RCT **Setting:** general practices from across Northamptonshire, UK
Participants	**Expected:** 210 **Inclusion criteria:** (1) male or female and aged 40 - 74 years, inclusive, (2) prescribed a statin medication for primary prevention of CVD that was still active, at least 12 months prior to enrolment, (3) total cholesterol level ≥ 5.0 mmol/L at enrolment, (4) able to speak and read English to participate effectively in the group education programme, (5) willing and able to attend education sessions and clinic visits, (6) access to a mobile phone, (7) willing and able to give informed consent, (8) willing to allow their GP to be notified of participation in the study

Byrne 2018 *(Continued)*

	Exclusion criteria: (1) no pre-existing CVD, (2) no inherited lipid disorder, (3) no established type 1 or type 2 diabetes, (4) no women who were pregnant (self-reported), and (5) no participation in another clinical intervention study in the 12 weeks prior to enrolment
Interventions	**Intervention:** Bespoke patient-centred Education Programme which will address CVD risk and explore participants' perceptions of the risk. The programme will use current evidence based information to provide advice on how to make positive behavioural change and assist participants to set achievable goals. The programme is delivered by 2 trained educators (at least 1 of them will be registered HCP) in a group session of 8 - 10 participants. Regular SMS (Short Message Service) reminder and validated motivation text messages will also be sent to participants after completion of the education session. Message delivery will be automated and unidirectional. The text messages will begin within a week of the second education session and will last for a total of 44 weeks **Control:** The control group continued with their usual GP care for lifestyle and medication advice for the primary prevention of CVD
Outcomes	**Primary outcome:** medication adherence to statins at 12 months; the primary measure is a urine-based biochemical measure involving a novel assay to test for statin and anti-hypertensive levels in urine samples **Secondary outcomes:** 1. CVD score: Variables are collected by the study and calculated by online version of QRISK, 2. TC (total cholesterol), HDL (High Density Lipoprotein), TC:HDL ratio: Non-fasting blood test taken at study clinic visits, 3. Blood pressure: Taken at study clinic visits, 4. BMI: Calculated using height and weight taken, 5. Waist-to-hip ratio: Waist and hip measurements will be used to calculate a waist-to-hip ratio 6. The following questionnaires will be used: 6.1. Self-reported history of smoking using a standard question format, 6.2. Fruit and vegetable consumption using the food frequency section of the validated 5-A-Day Consumption and Evaluation Tool (FACET) which is recommended by the Department of Health will be used to determine dietary intake in conjunction with a NHS Portion Size Guide, 6.3. The validated Quality of Life Questionnaire (15D), 6.4. The EQ5D as a validated measure of health status, 6.5. The validated International Physical Activity Questionnaire (short form) or IPAQ to obtain internationally-comparable data on health–related physical activity, 6.6. The Patient Activation Measure (PAM) as a validated measure of patient readiness for health behaviour change, 6.7. The Beliefs about Medicines Questionnaire (BMQ) 37 and the Brief Illness Perception Questionnaire (IPQ) will be used as validated measures of health and medication beliefs, 7. Medication adherence to antihypertensives measured at baseline and 12 months by the following ways: 7.1. Patient self-report (Morisky 8-item Medication Adherence Scale), 7.2. Levels of statins in urine sample; updated 14 June 2018: Levels of anti-hypertensive in urine sample
Starting date	May 2016
Contact information	Kamlesh Khunti kk22@leicester.ac.uk
Notes	ISRCTN16863160

Midlöv 2020

Study name	PERson-centredness in hypertension management using information technology (PERHIT): a protocol for a randomised controlled trial in primary health care
Methods	**Design:** 2-arm, parallel RCT **Setting**: Sweden; Primary healthcare centres in 4 Swedish counties (Skane, Vasta Gotaland, Ostergotland, Jonkoping) surrounding the 3 participating universities (Lund, Gothenburg and Linkoping) were used as clinical sites
Participants	**Expected:** 900

Midlöv 2020 *(Continued)*

	Inclusion criteria: Aged 18 or older; diagnosis of hypertension; on treatment with at least 1 antihypertensive drug; understanding of Swedish **Exclusion criteria:** Secondary hypertension according to medical records; terminal illness; pregnancy-induced hypertension; cognitive impairment; impaired vision (not able to read messages on mobile phone); psychotic disease
Interventions	**Intervention:** Participants are given a baseline assessment before being randomised into intervention or control groups. The intervention group is given instructions on how to use the onlinePERHIT system, how to measure blood pressure, log into the database and see their graphs. The PERHIT system includes (1) a module for self-reporting well-being, symptoms, lifestyle, medication intake and side effects of medication; (2) daily home BP and pulse measurements with a validated BP monitor; (3) tailored weekly motivational messages to encourage lifestyle changes and (4) web-based dash- board to enable participants, as well as physicians and nurses, to examine graphs for visualisation of the participant's BP in relation to the self-reports. This system is also tailored to each individual patient's need. At the end of the 8 weeks there will be a follow-up consultation with a set of questionnaires to fill in, and again after 1 year **Control:** Normal treatment with follow-up appointments after 8 weeks and a year
Outcomes	**Primary outcome**: Change in systolic blood pressure in participants with hypertension after 8 weeks and 1 year of using PERHIT **Secondary outcomes**: Change in person-centredness, daily life activities, awareness of risk and health care after 8 weeks and 1 year of using PERHIT
Starting date	October 2018
Contact information	Patrik MidLov: patrik.midlov@med.lu.se
Notes	ClinicalTrials.gov: NCT03554382

NCT03973931

Study name	Personalised patient data and behavioural nudges to improve adherence to chronic cardiovascular medications
Methods	**Design:** 4-arm randomised parallel RCT **Setting:** Denver USA- three health care systems in metro Denver: VA Eastern Colorado Health Care System (VA), Denver Health and Hospital Authority, and UCHealth, USA
Participants	**Expected:** 5000 **Inclusion criteria:** 18 - 89 years; Patients with the following cardiovascular conditions and respective medication classes- Hypertension (beta-blockers [B-blockers]) calcium channel blocker [CCB], angiotensin converting enzyme inhibitors (ACEi), angiotensin receptor blockers [ARB], or Thiazide diuretic, Hyperlipidaemia (HMG CoA reductase inhibitor [Statins]), diabetes (alpha-glucosidase inhibitors, biguanides, DPP-4 inhibitors, sodium glucose transport inhibitor, meglitinides, sulfonylureas, thiazolidinediones, or statins; coronary artery disease P2Y12 inhibitor [clopidogrel, ticagrelor, prasugrel, ticlopidine], B-blockers, ACEi or ARB or statins), atrial fibrillation (Direct oral anticoagulants, B-blockers, CCB) **Exclusion criteria:** do not have a mailing address listed in EHR; do not have a landline or cell phone listed in EHR; currently pregnant if denoted in the EHR at the time of the data pull; a mailing address outside of the state of Colorado; do not speak either English or Spanish
Interventions	**Intervention:**

NCT03973931 *(Continued)*

	Group 1: Generic Nudge- A generic reminder text will be delivered to participants to refill their medication at days 1, 3, 5, 7 and 10 after they have been labelled as non-adherent Group 2: Optimised Nudge- An optimised nudge text will be delivered to participants to remind them to refill their medications at days 1, 3, 5, 7 and 10 after they have been labelled as non-adherent Group 3: Optimised nudge plus AI Chat Box An optimised nudge text will be delivered to participants to remind them to refill their medications at days 1 and 3 after they have been labelled as non-adherent. If the participant has not filled their medication on days 5 and 7, in addition to receiving an optimised nudge text, an AI will conduct interactive chat via a chat bot to assess barriers filling the medication. If they still have not filled the medication, they will receive another message on day 10 **Control:** Usual care
Outcomes	**Primary outcome:** medication adherence defined by the proportion of days covered (PDC) using pharmacy refill data (measured up to 12 months after intervention) **Secondary outcomes:** Blood pressure; Low-density lipoproteins (LDL); Haemoglobin A1c; Hospitalisations rate (cardiovascular clinical events); Emergency Department admission rates (cardiovascular clinical events); percutaneous coronary intervention (PCI) rates, (cardiovascular clinical events); coronary artery bypass graft (CABG) rates, (cardiovascular clinical events); cardioversion rates (cardiovascular clinical events); All-cause hospitalisations (hospitalisations); Implementation costs (costs); healthcare utilisation costs (costs). All measured up to 12 months after intervention
Starting date	July 2019
Contact information	Lisa Sandy lisa.sandy@ucdenver.edu
Notes	ClinicalTrials.gov NCT03973931

Redfern 2014

Study name	A randomised controlled trial of a consumer-focused e-health strategy for cardiovascular risk management in primary care: the Consumer Navigation of Electronic Cardiovascular Tools (CONNECT)
Methods	**Design:** 2-arm, parallel RCT **Setting:** 65 Australian General Practices and Aboriginal Community Controlled Health Services
Participants	**Expected:** 2000 **Inclusion criteria:** consenting adults (> 18 years) with access to the Internet at least once a month via mobile phone, tablet or computer who are at moderate-to-high risk of a CVD event will be included Moderate-to-high CVD risk is defined as any of the following: 1. 5-year CVD risk ≥ 10% using the Framingham risk equation; 2. a clinically high-risk condition (Aboriginal/Torres Strait Islander and aged > 75 years, diabetes and age > 60 years, diabetes and albuminuria, epidermal growth factor receptor 7.5 mmol); 3. an established CVD diagnosis (ischaemic heart disease, stroke/transient ischaemic attack and peripheral vascular disease) **Exclusion criteria:** severe intellectual disability or if they have insufficient English knowledge to provide written informed consent
Interventions	**Intervention:** CONNECT programme, a consumer-focused e-health strategy aimed at assisting with the management and prevention of CVD in addition to usual care. Programme components fo-

Redfern 2014 *(Continued)*

	cus on cardiovascular risk assessment, medication adherence, lifestyle change and seamless patient-provider communication **Control group:** Usual healthcare. No access to the portal; however, at the end of study, all participants (control and intervention) will be offered portal access for a maximum of 12 months
Outcomes	**Primary outcome:** proportion of participants meeting the Australian guideline BP and lipid targets; BP 140/90 mmHg for all except those with CVD, diabetes or albuminuria for whom the target BP is 130/80 mmHg **Secondary outcomes**: proportion meeting guideline-recommended BP and LDL-C targets separately; difference in mean SBP and DBP at the end of study; difference in mean cholesterol levels at end of study (TC, LDL-C and HDL-C); difference in mean BMI and waist circumference at the end of study; difference in health literacy scores (HLQ51 and the eHEALS52) at end of study; cardiovascular and renal events, new-onset diabetes - self-report and confirmed with medical records; physical activity - WHO Global Physical Activity Questionnaire; point abstinence in smoking (≤ 5 cigarettes in the previous 7 days or recent smoking according to assessment using carbon monoxide meter); fruit and vegetable intake, fish, salt and saturated fat intake - self-report portions consumed in 7 days prior and compared with published guidelines recommendations; cardioprotective medication adherence - self-report and verified by medical record and pharmaceutical benefits scheme data; all-cause mortality - medical record; hospital readmissions - self-report and verified by medical record; health-related quality of life - EQ5D (version 5L with Australian standardised weights)
Starting date	17 October 2014
Contact information	Dr Julie Redfern; jredfern@georgeinstitute.org.au
Notes	Clinical Trials registration number ACTRN12613000715774.

Schroeder 2019

Study name	An Interactive Voice Response and text message intervention to improve blood pressure control among individuals with hypertension receiving care at an urban Indian health organization: protocol and baseline characteristics of a pragmatic randomized controlled trial
Methods	**Design:** 2-arm parallel RCT **Setting:** Albuquerque, New Mexico:First Nations Community HealthSource - a non-profit, urban Indian community-based health and human services organization
Participants	**Expected:** 295 **Inclusion criteria:** Aged 21 - 79; Have a diagnosis of hypertension (considered to be any of the following: : (1) having 2 visits with a hypertension diagnosis on different days, (2) having 1 visit with a hypertension diagnosis and 1 medication order, (3) having 1 visit with a hypertension diagnosis and 1 elevated blood pressure, or (4) having 2 consecutive elevated blood pressures on different day); at least 2 prior visits to FNCH with blood pressure measurements; , at least 1 of which took place in the 24 months before recruitment **Exclusion criteria:** Another preferred site of primary care; significant impairment of vision and hearing; life-limiting illnesses such as advanced cancer; renal dialysis; receipt of home health care with blood pressure monitoring and/or assistance with administration of medications; hospice services or residence in a nursing home; dementia; pregnancy at the time of recruitment; current homelessness; no landline or cellular phone access; or inability to understand English or Spanish
Interventions	**Intervention:** Individuals randomised to the intervention group could opt to receive either automated text messages or automated phone calls in either English or Spanish. The messages include reminders of upcoming appointments at First Nations Community HealthSource, requests

Schroeder 2019 *(Continued)*

	to reschedule recently missed appointments, monthly reminders to refill medications, and weekly motivational messages to encourage self-care, appointment-keeping, and medication-taking for hypertension. Individuals in the intervention arm could opt to nominate a care partner to also receive notices of upcoming and missed appointments. Individuals in the intervention arm were also offered a home blood-pressure monitor. Follow-up visits will be conducted at 6 months and 12 months where they filled in a health survey and had a blood pressure measurement taken **Control:** Standard care
Outcomes	**Primary outcome:** Change in mean systolic blood pressure between baseline and 12 months **Secondary outcomes:** Change in diastolic blood pressure, self-reported adherence, and the proportion of missed clinic appointments between intervention and control groups
Starting date	April 2017
Contact information	Emily B Schroeder: emily.b.schroeder@kp.org
Notes	ClinicalTrials.gov NCT03135405;

SMASH 2017

Study name	Patient centred health technology medication adherence program for African American hypertensives (SMASH)
Methods	**Design:** 2-arm Parallel RCT **Setting:** Medical University of South Carolina, USA
Participants	**Expected:** 204 **Inclusion criteria:** 21 - 59 year old; African-American or black; prescribed medication(s) only for HTN; medication possession ratio (MPR) < .85 for last 3 months; uncontrolled HTN (SBP ≥ 130 mmHg) based upon last clinic visit within previous 12 months, initial clinic screening and subsequent baseline recruitment evaluation following 1 month med intake screening with score of < .85; 24-hour SBP ≥ 130 mmHg on clinic screening and subsequent recruitment evaluation; ability to speak, hear and understand English; able to take their own BP and self-administer medications; owns smart phone with data plan; primary care provider's assent that patient is able to participate **Exclusion criteria:** No other known chronic disease (e.g. chronic kidney disease (GFR < 50 mL/1.7 m^2/min; diabetes (type 1 or 2); renal dialysis; cancer diagnosis or treatment in past 2 years; prior CV event such as heart attack, congestive heart failure, arterial stent, coronary artery bypass graft psychiatric illness; Beck Depression Inventory score > 13; ongoing substance abuse (e.g. > 21 drinks/week); planned pregnancy; vulnerable populations such as pregnant or nursing women, prisoners, and institutionalised individuals
Interventions	**Intervention:** participants are randomised into SMASH or enhanced standard care groups. The SMASH group will receive reminders in the form of auditory and visual reminders from a pill-monitoring device when their medication dose is due. They will monitor their blood pressure at home and will receive tailored motivational text messages based upon levels of adherence. All participants will complete 5 study visits where BP, medication possession ratios, and surveys will be completed. 24-hour ambulatory blood pressure (ABP) monitoring will be performed every 6 months (4 times) during the study. The intervention will last 6 months with follow-up for 1 year **Control:** Enhanced standard care - Use the pill-monitoring device without reminder functions enabled and will receive text messages on topics of healthy lifestyles not related to medication adherence and hypertension

SMASH 2017 *(Continued)*

Outcomes	**Primary outcome:** Percent of participants meeting JNC8 Guidelines for BP control (< 140/90) (Time frame: at 6 months at the end of intervention); Percent of participants with medication adherence to > .90 **Secondary outcomes:** Changes in medication adherence self-efficacy (Time frame: months 3, 6, of intervention period and at months 12 and 18 during follow-up period); percent achieving and sustaining 24-hr BP control (< 130/80 mmHg) (Time frame: month 6 of intervention period and at month 6 and 12 of follow-up period); changes in autonomous motivation (Time frame: months 3, 6 of intervention period and at months 6 and 12 of follow-up period); percent of participants achieving and maintaining JNC8 Guidelines for BP control (< 140/90) (Time frame: month 6 of intervention and months 6 and 12 of follow-up period); percent of participants achieving and maintaining medication adherence > .90. (Time frame: Months 3, 6 of intervention period and at months 6 and 12 of follow-up period)
Starting date	April 2017
Contact information	Jessica Chandler, Medical University of South Carolina
Notes	ClinicalTrials.gov Identifier: NCT03454308

TEACH 2018

Study name	Text Messaging and Cardiovascular Health in diabetes mellitus (TEACH)
Methods	**Design:** 2-arm parallel RCT **Setting:** Nanfang Hospital of Southern Medical University recruiting from Guangzhou, Guangdong, China
Participants	**Expected:** 800 **Inclusion criteria:** 18 - 80 years; People with poorly-controlled type 2 diabetes who are undergoing routine treatment (defined as HbA1c ≥ 7% or HbA1c ≥ 7.5% if combined with clinical cardiovascular disease) have at least 1 risk factor for other cardiovascular disease (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or low-density lipoprotein cholesterol ≥ 100 mg/dL) or clinical atherosclerotic cardiovascular disease (acute coronary syndrome, ischaemic stroke, transient ischaemic attack or peripheral arterial disease); have access to a smartphone and be able to receive and read text messages **Exclusion criteria:** in functional New York Heart Association class III or IV, and were on haemodialysis; pregnant women or women planning to become pregnant; cannot be followed up for 12 months (due to health or migration); can provide written informed consent
Interventions	**Intervention**: The intervention group will receive text messages alongside usual care. Text messages will target lifestyle recommendation, glucose control, blood pressure control, healthy eating, medication adherence, physical activity and smoking cessation. Each message will be sent on 6 of 7 randomly-selected weekdays and arrive at random times of the day during working hours. This will continue for 12 months **Control:** Usual care
Outcomes	**Primary outcome:** Combined changes in HbA1C, SBP and LDL-cholesterol levels, simultaneous modelled using a scaled marginal model. These will be measured at month 3, 6 and 12 of the study **Secondary outcomes:** Net change of CVD risk factors (glycated haemoglobin [HbA1C], systolic blood pressure [SBP], and LDL-cholesterol), and the proportion of participants with HbA1C < 7% (<

TEACH 2018 *(Continued)*

	7.5% if with clinical CVD), BP < 140/90 mmHg, and LDL-cholesterol < 100 mg/dL, and net change in estimated 10-year risk of CHD and CVD. These will be measured at month 3, 6 and 12 of the study
Starting date	November 2018
Contact information	Huijie Zhang Huijiezhang2005@126.com
Notes	ClinicalTrials.gov NCT03724526

Venkateshmurthy 2018

Study name	m-Power Heart Project - a nurse care co-ordinator-led, mHealth-enabled intervention to improve the management of hypertension in India: study protocol for a cluster-randomised trial
Methods	**Design:** 2-arm, cluster-RCT **Setting:** 12 CHCs (secondary-level public health facility which offers speciality services) in the Visakhapatnam district (India)
Participants	**Expected:** 1876 **Inclusion criteria:** Age 30+; on treatment for hypertension or opportunistically screened and diagnosed with a BP ≥ 160/90 mmHg **Exclusion criteria:** Pregnant women; unwilling/unable to produce written informed consent; diagnosed with malignancy or life-threatening condition; currently enrolled in other trials; plans to move residence in the year ahead
Interventions	**Intervention:** Participants are given use of the electronic decision-support system (EDSS) which is installed onto a tablet. EDSS considers participant age, blood pressure levels, comorbidities and current medication to suggest best course of treatment for the participant. EDSS also recommends lifestyle changes (reduction of salt, increased consumption of fruit and vegetables, quitting tobacco and alcohol); it will also facilitate data management by storing the information electronically and providing a structured follow-up plan for each participant. Nurse Care co-ordinators (NCCs) will also measure BP, provide counselling of lifestyle changes, facilitate treatment and follow up and promote adherence to medication. NCCs will be supported by automated text messages to the participant, conveying information about hypertension and its management in the participant's local language (risk factors, importance of lifestyle changes, regular intake of medication, reminders of follow up visits, etc.) **Control:** Standard hypertension care
Outcomes	**Primary outcome**: The difference in the mean change of SBP, from baseline to 12 months, between the intervention and the standard treatment arms **Secondary outcomes:** The difference in mean change of DBP; difference in the proportion of participants with controlled blood pressure (< 140/90 mmHg); difference in mean change of fasting blood sugar, HbA1C, eGFR, and albumin-to-creatinine ratio; difference in the proportion of participants visiting the CHC regularly (number of actual visits to the CHC/number of visits suggested by the EDSS > 80%); difference in proportion of participants compliant to antihypertensive medications; cost effectiveness of intervention versus enhanced care. All outcomes are assessed at 12 months
Starting date	May 2017
Contact information	Dorairaj Prabhakaran; dprabhakaran@ccdcindia.org

Venkateshmurthy 2018 *(Continued)*

Notes	ClinicalTrials.gov NCT03164317

Xu 2017

Study name	A co-ordinated PCP-Cardiologist Telemedicine Model (PCTM) in China's community hypertension care: study protocol for a randomized controlled trial
Methods	**Design:** 3-arm, parallel RCT **Setting:** 4 CHCs in XuHui District in Shanghai, China
Participants	**Expected:** 330 **Inclusion criteria:** aged ≥ 21 years; clinical diagnosis of hypertension with uncontrolled BP in the previous 3 months, currently taking or about to take antihypertensive medications; received high school or above level of education; active user of smartphone (Android or Apple) and mobile Apps; mean of 3 BP measurements during the screening visit at the CHC ≥ 140/90 mmHg, or ≥ 130/80 mmHg if the person has diabetes or renal diseases; being able to give informed consent **Exclusion criteria:** acute coronary syndrome; heart failure; cardiac arrhythmia; stroke within the past 3 months; renal failure; cancer; dementia, severe or acute psychiatric illness; pregnancy or intention to be pregnant in the next 18 months; hospitalisation within 3 months; participation in another clinical trial; arm circumference > 32 cm that may affect the accuracy of BP measurement due to cuff size limit of the telemonitors and unwillingness to comply with the 12-month intervention duration
Interventions	**Intervention:** Group 1: 'Self-management' (BP telemonitor and app-based self-management supports; patient proficiency training) Group 2: 'PCTM intervention' (BP telemonitor and app-based self-management supports; patient proficiency training; PCP and cardiologist training of using web-based analytics; proactive and interactive care by PCPs and cardiologists) **Control group:** management by PCPs at the registered CHCs as usual
Outcomes	**Primary outcome:** changes in mean SBP from baseline to 12 months measured using the BP telemonitor (Bliss BL928). The 12-month BP readings will be determined by taking the mean of 3 BP measurements at the follow-up visit to the CHC **Secondary outcomes:** changes in mean DBP from baseline to 12 months; hypertension control rate from baseline to 6 and 12 months; hypertension control rate defined as BP < 140/90 mmHg or < 130/80 mmHg (people with diabetes or renal diseases) following the national guidelines; changes in measures related to hypertension complications (HbA1c, BMI and lipid levels) from baseline to 6 and 12 months; antihypertensive medication adherence at baseline and 12 months assessed by self-report, 8-item Morisky Medication Adherence Scale modified to focus on BP drugs
Starting date	September 2016
Contact information	Contact: Lei Xu, Master; +86-21-32260806; waqyl@126.com Contact: Kai Liu, Doctor; +86-18918656956; liuk@carelinker.com
Notes	ClinicalTrials.gov, NCT02919033

Zhang 2020

Study name	Strategy of blood pressure intervention in the elderly hypertensive patients (STEP): Rationale, design, and baseline characteristics for the main trial
Methods	**Design:** 2-arm parallel RCT **Setting:** 42 clinical centres (hospitals with a local study group for hypertension control) from 23 provinces throughout China
Participants	**Expected:** 8511 **Inclusion criteria:** SBP between 140 and 190 mmHg in 3 screening visits or currently receiving anti-hypertensive treatment; between 60 - 80 years of age; Han ethnicity; signed the written informed consent **Exclusion criteria**: SBP ≥ 190 or DBP < 60 mmHg; diagnosed with secondary hypertension; history of larger atherosclerotic cerebral infarction or haemorrhagic stroke; hospitalisation for MI within the last 6 months; coronary revascularisation (PCI or CABG) within the last 12 months; planned to perform PCI or CABG in the next 12 months; history of sustained atrial fibrillation or ventricular arrhythmias at entry influencing the measurement of electronic blood pressure; NYHA class III - IV heart failure or hospitalisation for exacerbation of chronic heart failure at entry; severe valvular disease or valvular disease likely to require surgery or percutaneous valve replacement during the trial; hypertrophic cardiomyopathy (HCM); dilated cardiomyopathy; rheumatic heart disease; congenital heart disease; uncontrolled diabetes mellitus (serum fasting glucose ≥ 200 mg/dL [11.1 mmol/L], glycated haemoglobin [HbA1] > 8%); severe liver or kidney dysfunction (ALT ≥ 3 times the upper limit of normal value, or end-stage renal disease on dialysis or eGFR < 30 ml/min/1.73 m, or serum creatinine > 2.5 mg/dL [> 221 µmol/L]); severe somatic disease such as cancer; severe cognitive impairment or mental disorders; participating in other clinical trials
Interventions	**Intervention:** Participant underwent a baseline survey looking at weight, height, waist circumference, smoking status, alcohol intake, medical history and current medications, frailty and cognitive dysfunction, anti-hypertensive medication adherence. A 12-lead ECG was also requested from the last 3 months. These participants were then randomised to receive intensive treatment (110 SBP < 130 mmHg) or standard treatment (130 SBP < 150 mmHg) and medication was then prescribed accordingly. They were followed up monthly for 3 months and then every 3 months for the follow-up period. The 42 clinical centres were then split in a 1:1 ratio so that half received app management intervention. Each intervention participant received a Omron HEM- 9200 automatic blood-pressure monitor and had access to the Hypertension Doctor App. The app allows patients to upload blood pressure readings and aims to help medication adherence (using antihypertensive treatment plan, graphic data of home blood pressure during the follow-up, interactive communications between patients and physicians, and cardiovascular health education) **Control**: Usual care by physicians at clinical office visits
Outcomes	**Primary outcome:** Assess whether intensive treatment (a goal of 110 ≤ SBP < 130 mmHg) will provide more benefits in lowering CVD risk than standard treatment (a goal of 130 ≤ SBP < 150 mmHg) in Chinese population aged 60 – 80 years **Secondary outcomes:** Evaluate whether the smartphone-based blood pressure app management strategy would improve blood pressure control and reduce the CVD events during the follow-up
Starting date	January 2017
Contact information	W Zhang: zhangweili1747@yahoo.com
Notes	ClinicalTrials.gov NCT03015311

BMI: body mass index; BP: blood pressure; CHC: community healthcare centre; CKD: Chronic Kidney Disease; CVD: cardiovascular disease; DBP: diastolic blood pressure; GP: general practitioner; HbA1c: glycated haemoglobin; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; MARS: Medication Adherence Report Scale; mHealth: mobile health; MoH: Minister of Health;

NIHR: National Institute for Health Research; PCC: primary care centre; PCP: primary care physician; PDC: proportion of days covered; RCT: randomised controlled trial; SBP: systolic blood pressure; SMS: short messaging service; TC: total cholesterol; WHO: World Health Organization.

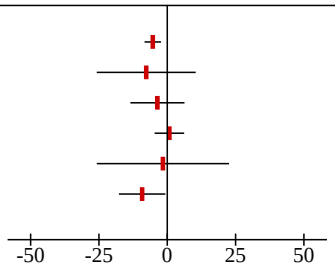
DATA AND ANALYSES

Comparison 1. Mobile phone intervention versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Change in low-density lipoprotein cholesterol (mg/dL)	5		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.2 Change in total cholesterol (mg/dL)	4		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.3 Change in high-density lipoprotein cholesterol (mg/dL)	3		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.4 Change in systolic blood pressure (mmHg)	13		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.5 Pooled change in systolic blood pressure (mmHg)	2	1494	Mean Difference (IV, Fixed, 95% CI)	-1.55 [-3.36, 0.25]
1.6 Change in diastolic blood pressure (mmHg)	11		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.7 Controlled blood pressure	7		Odds Ratio (IV, Fixed, 95% CI)	Totals not selected
1.8 Pooled controlled blood pressure	2	1494	Odds Ratio (IV, Fixed, 95% CI)	1.32 [1.06, 1.65]
1.9 Combined fatal and non-fatal CVD events	4		Odds Ratio (IV, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1: Mobile phone intervention versus control, Outcome 1: Change in low-density lipoprotein cholesterol (mg/dL)

Study or Subgroup	MD	SE	Intervention Total	Control Total	Mean Difference IV, Fixed, 95% CI
Choudhry 2018 (1)	-5.3	1.5306	1467	1503	-5.30 [-8.30 , -2.30]
Gulayin 2019 (2)	-7.7	9.2349	75	58	-7.70 [-25.80 , 10.40]
Gulayin 2019 (3)	-3.6	5.0511	58	54	-3.60 [-13.50 , 6.30]
Liu 2015	0.77	2.7603	238	351	0.77 [-4.64 , 6.18]
Morillo-Verdugo 2018 (4)	-1.6	12.3373	29	19	-1.60 [-25.78 , 22.58]
Párraga-Martínez 2017	-9.2	4.3368	155	149	-9.20 [-17.70 , -0.70]



Footnotes

(1) endline LDL (results in paper account for clustering)

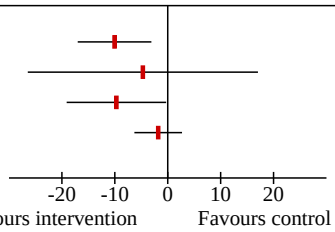
(2) Subgroup: High CVD risk. Framingham 10 year risk score ≥ 20%

(3) Subgroup: Moderate CVD risk. Framingham 10 year risk score 10% - 20%, or diabetic

(4) endline LDL (note: intervention SD reported in paper as 4.8, control SD reported as 41.8 - assumed intervention typo and given both groups SD c

Analysis 1.2. Comparison 1: Mobile phone intervention versus control, Outcome 2: Change in total cholesterol (mg/dL)

Study or Subgroup	MD	SE	Intervention Total	Control Total	Mean Difference IV, Fixed, 95% CI
Liu 2015	-10.05	3.5511	238	351	-10.05 [-17.01 , -3.09]
Morillo-Verdugo 2018 (1)	-4.7	11.0963	29	24	-4.70 [-26.45 , 17.05]
Párraga-Martínez 2017	-9.7	4.796	155	149	-9.70 [-19.10 , -0.30]
Prabhakaran 2019 (2)	-1.8	2.296	1637	1687	-1.80 [-6.30 , 2.70]



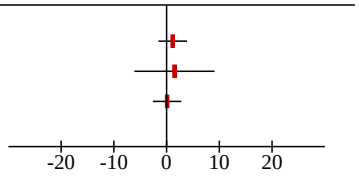
Footnotes

(1) endline total cholesterol

(2) results reported in paper adjusted for clustering

Analysis 1.3. Comparison 1: Mobile phone intervention versus control, Outcome 3: Change in high-density lipoprotein cholesterol (mg/dL)

Study or Subgroup	MD	SE	Intervention Total	Control Total	Mean Difference IV, Fixed, 95% CI
Liu 2015	1.16	1.3827	238	351	1.16 [-1.55 , 3.87]
Morillo-Verdugo 2018 (1)	1.5	3.8809	29	20	1.50 [-6.11 , 9.11]
Párraga-Martínez 2017	0.1	1.3776	155	149	0.10 [-2.60 , 2.80]

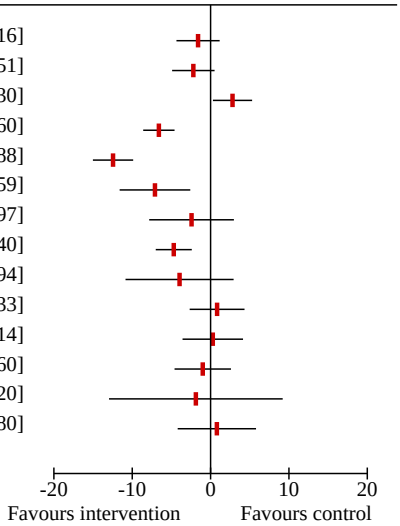


Footnotes

(1) endline HDL

Analysis 1.4. Comparison 1: Mobile phone intervention versus control, Outcome 4: Change in systolic blood pressure (mmHg)

Study or Subgroup	MD	SE	Intervention Total	Control Total	Mean Difference IV, Fixed, 95% CI
Bobrow 2016 (1)	-1.6	1.4061	457	229	-1.60 [-4.36 , 1.16]
Bobrow 2016 (2)	-2.2	1.382	457	229	-2.20 [-4.91 , 0.51]
Choudhry 2018 (3)	2.8	1.2755	529	486	2.80 [0.30 , 5.30]
He 2017 (4)	-6.6	1.0204	709	648	-6.60 [-8.60 , -4.60]
Liu 2015 (5)	-12.45	1.3112	238	351	-12.45 [-15.02 , -9.88]
Logan 2012 (6)	-7.1	2.3	54	51	-7.10 [-11.61 , -2.59]
Márquez Contreras 2019 (7)	-2.43	2.7571	24	25	-2.43 [-7.83 , 2.97]
McManus 2018	-4.7	1.1735	327	348	-4.70 [-7.00 , -2.40]
Morillo-Verdugo 2018 (5)	-3.96	3.519	29	24	-3.96 [-10.86 , 2.94]
Párraga-Martínez 2017	0.83	1.7857	155	149	0.83 [-2.67 , 4.33]
Peiris 2019 (4)	0.28	1.9694	4348	4294	0.28 [-3.58 , 4.14]
Prabhakaran 2019 (4)	-1	1.8368	1637	1687	-1.00 [-4.60 , 2.60]
Saleh 2018 (8)	-1.88	5.6537	74	68	-1.88 [-12.96 , 9.20]
Tobe 2019	0.8	2.5511	64	58	0.80 [-4.20 , 5.80]



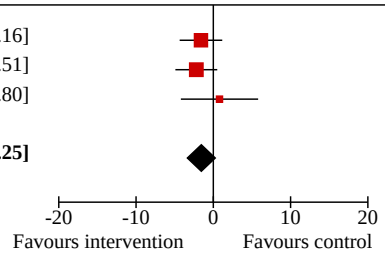
Footnotes

(1) Interactive messaging versus control (endline BP, control group halved)
(2) Information only messaging versus control (endline BP, control group halved)
(3) Endline blood pressure (results reported in report account for clustering)
(4) results reported in paper account for clustering
(5) endline blood pressure
(6) Daytime systolic blood pressure measurement
(7) effective sample size based on (icc: 0.055 from Singh 2015, average cluster size: 37)
(8) endline blood pressure (effective sample size based on icc: 0.055 from Singh 2015, average cluster size: 147)

Analysis 1.5. Comparison 1: Mobile phone intervention versus control, Outcome 5: Pooled change in systolic blood pressure (mmHg)

Study or Subgroup	MD	SE	Intervention Total	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Bobrow 2016 (1)	-1.6	1.4061	457	229	42.8%	-1.60 [-4.36 , 1.16]
Bobrow 2016 (2)	-2.2	1.382	457	229	44.3%	-2.20 [-4.91 , 0.51]
Tobe 2019	0.8	2.5511	64	58	13.0%	0.80 [-4.20 , 5.80]
Total (95% CI)			**978**	**516**	**100.0%**	**-1.55 [-3.36 , 0.25]**

Heterogeneity: Chi² = 1.07, df = 2 (P = 0.59); I² = 0%
Test for overall effect: Z = 1.69 (P = 0.09)
Test for subgroup differences: Not applicable

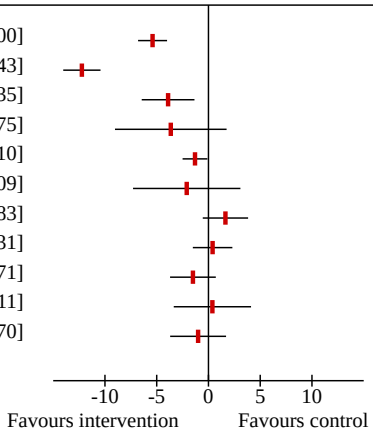


Footnotes

(1) Interactive messaging versus control (endline BP, control group halved)
(2) Information only messaging versus control (endline BP, control group halved)

Analysis 1.6. Comparison 1: Mobile phone intervention versus control, Outcome 6: Change in diastolic blood pressure (mmHg)

Study or Subgroup	MD	SE	Intervention Total	Control Total	Mean Difference IV, Fixed, 95% CI
He 2017 (1)	-5.4	0.7143	709	648	-5.40 [-6.80 , -4.00]
Liu 2015 (2)	-12.23	0.9184	238	351	-12.23 [-14.03 , -10.43]
Logan 2012 (3)	-3.9	1.3	54	51	-3.90 [-6.45 , -1.35]
Márquez Contreras 2019 (4)	-3.64	2.7505	17	18	-3.64 [-9.03 , 1.75]
McManus 2018	-1.3	0.6123	328	348	-1.30 [-2.50 , -0.10]
Morillo-Verdugo 2018 (5)	-2.1	2.6462	29	24	-2.10 [-7.29 , 3.09]
Párraga-Martínez 2017	1.64	1.1174	155	149	1.64 [-0.55 , 3.83]
Peiris 2019 (1)	0.4	0.9745	4348	4294	0.40 [-1.51 , 2.31]
Prabhakaran 2019 (6)	-1.5	1.1271	193	199	-1.50 [-3.71 , 0.71]
Saleh 2018 (7)	0.38	1.9051	47	43	0.38 [-3.35 , 4.11]
Tobe 2019	-1	1.3776	64	58	-1.00 [-3.70 , 1.70]

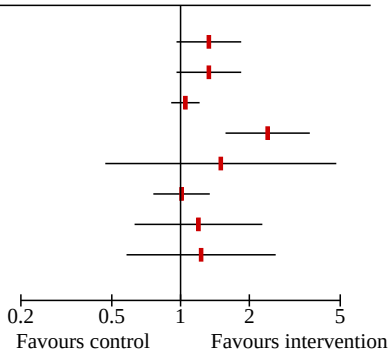


Footnotes

(1) results reported in paper account for clustering
(2) endline blood pressure
(3) Daytime diastolic blood pressure measurement
(4) effective sample size based on (icc: 0.091 from Singh 2015, average cluster size: 37)
(5) blood pressure at endline
(6) blood pressure at endline (effective sample size based on icc: 0.091 from Singh 2015, average cluster size: 83)
(7) endline blood pressure (effective sample size based on icc: 0.091 from Singh 2015, average cluster size: 147)

Analysis 1.7. Comparison 1: Mobile phone intervention versus control, Outcome 7: Controlled blood pressure

Study or Subgroup	log[OR]	SE	Intervention Total	Control Total	Odds Ratio IV, Fixed, 95% CI
Bobrow 2016 (1)	0.2852	0.1663	457	229	1.33 [0.96 , 1.84]
Bobrow 2016 (2)	0.2852	0.1663	457	229	1.33 [0.96 , 1.84]
Choudhry 2018 (3)	0.0488	0.073	2038	2040	1.05 [0.91 , 1.21]
He 2017 (4)	0.8778	0.2167	201	183	2.41 [1.57 , 3.68]
Morillo-Verdugo 2018 (5)	0.4055	0.594	28	24	1.50 [0.47 , 4.81]
Peiris 2019 (6)	0.01	0.1451	4348	4294	1.01 [0.76 , 1.34]
Saleh 2018 (7)	0.1804	0.3285	81	75	1.20 [0.63 , 2.28]
Tobe 2019 (8)	0.207	0.3835	64	58	1.23 [0.58 , 2.61]



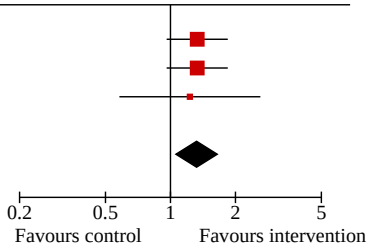
Footnotes

(1) Information only text messages (BP<140/90mmHg, control group halved)
(2) Interactive text messages (BP<140/90mmHg, control group halved)
(3) achieving good control on 'all eligible outcomes': Defined by hemoglobin A1c less than 8% (to convert to proportion of total hemoglobin, multipl
(4) BP<140/90mmHg (Calculated using effective sample sizes bases on ICC for blood pressure control reported in paper: 0.0415, and average cluste
(5) Cut off not stated: "The number of patients whose blood pressure levels were in accordance with their stated objectives"
(6) SBP<140mmHg (results in paper adjusted for clustering)
(7) BP<140/90 mmHg (effective sample size based on icc: 0.05 from Lee 2020, average cluster size: 147)
(8) BP<140/90mmHg or 130/80mmHg in diabetics

Analysis 1.8. Comparison 1: Mobile phone intervention versus control, Outcome 8: Pooled controlled blood pressure

Study or Subgroup	log[OR]	SE	Intervention Total	Control Total	Weight	Odds Ratio IV, Fixed, 95% CI
Bobrow 2016 (1)	0.2852	0.1663	457	229	45.7%	1.33 [0.96 , 1.84]
Bobrow 2016 (2)	0.2852	0.1663	457	229	45.7%	1.33 [0.96 , 1.84]
Tobe 2019 (3)	0.207	0.3835	64	58	8.6%	1.23 [0.58 , 2.61]
Total (95% CI)			**978**	**516**	**100.0%**	**1.32 [1.06 , 1.65]**

Heterogeneity: Chi² = 0.04, df = 2 (P = 0.98); I² = 0%
Test for overall effect: Z = 2.48 (P = 0.01)
Test for subgroup differences: Not applicable

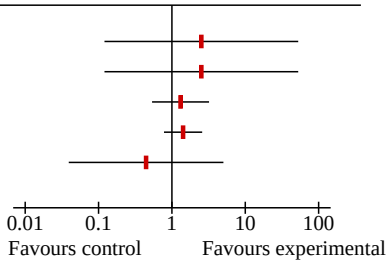


Footnotes

(1) Interactive text messages (BP < 140/90 mmHg, control group halved)
(2) Information only text messages (BP < 140/90 mmHg, control group halved)
(3) BP < 140/90 mmHg or 130/80 mmHg in diabetics

Analysis 1.9. Comparison 1: Mobile phone intervention versus control, Outcome 9: Combined fatal and non-fatal CVD events

Study or Subgroup	log[OR]	SE	Experimental Total	Control Total	Odds Ratio IV, Fixed, 95% CI
Bobrow 2016 (1)	0.9239	1.5513	457	229	2.52 [0.12 , 52.69]
Bobrow 2016 (2)	0.9239	1.5513	457	229	2.52 [0.12 , 52.69]
McManus 2018 (3)	0.2709	0.4562	327	348	1.31 [0.54 , 3.21]
Peiris 2019 (4)	0.3507	0.3057	951	940	1.42 [0.78 , 2.59]
Tobe 2019 (3)	-0.8109	1.2384	64	58	0.44 [0.04 , 5.03]



Footnotes

(1) Information only messaging versus control (control group halved) (CVD death)
(2) Interactive messaging versus control (control group halved) (CVD death)
(3) Non-fatal CVD events
(4) Non-fatal CVD events (results in paper adjusted for clustering)

ADDITIONAL TABLES

Table 1. Indirect measures of adherence

Trial	Outcome measure	Comparison	Intervention	Number (intervention)	Control	Number (Control)	Narrative results
Bobrow 2016 (1-year follow-up)	Proportion of days covered by dispensed BP medicine (prescription data)	Information-only SMS vs control	MD 83.3% (95% CI 69.3 to 91.7)	457	79.2% (95% CI 4.6 to 91.4)	458	Median difference 5.2, quartiles 1 - 3: 1.5 to 8.9; P = 0.006
		Interactive SMS vs control	MD 83.3% (95% CI 66.7 to 91.7)	457	79.2% (95% CI 64.6 to 91.4)	458	Median difference 3.8; quartiles 1 - 3: 0.03 to 7.6; P = 0.048
	Proportion of participants with proportion of days covered ≥ 80% (prescription data)	Information-only SMS vs control	63%	457	49.4%	458	Adjusted OR 1.86, 95% CI 1.39 to 2.49; P < 0.001
		Interactive SMS vs control	60%	457	49.4%	458	Adjusted OR 1.60, 95% CI 1.20 to 2.16; P = 0.002
	Self-reported medication adherence (score range 5 – 10)	Information-only SMS vs control	10 (quartiles 1 - 3: 9 to 10)	457	10 quartiles 1 - 3: 9 to 10)	458	Median difference 0.04, 95% CI −0.1 to 0.2; P = 0.70
		Interactive SMS vs control	10 (quartiles 1-3: 9 to 10)	457	10 (quartiles 1-3: 9 to 10)	458	Median difference 0.02, 95% CI −0.2 to 0.2; P = 0.80
Párraga-Martínez 2017 (2-year follow-up)	Proportion adherent to lipid-lowering medication according to self-reported medication adherence (measured using 'adapted Morisky-Green test')	—	77.2%	Disaggregated not reported	64.1%	Disaggregated not reported	P = 0.029 220 in total, not reported by group
He 2017 (18-month follow-up)	High adherence to BP medication (Morisky score = 8)	—	66.1%	629	53.0%	542	Risk difference[a]: 13.1%, 95% CI 7.0 to 19.2; P < 0.001
Gulayin 2019 (1-year follow-up)	Participants at moderate CVD risk: High adherence to lipid-lowering medication (Morisky score = 8)	—	46.9%	58	50.1%	54	Risk difference[a] −3.2, 95% CI −27.9 to 21.5); P = 0.7994

Table 1. Indirect measures of adherence *(Continued)*

	Participants at high CVD risk: High adherence to lipid- lowering medication (Morisky score = 8)	—	30.3%	75	45.8%	58	Risk difference −15.5, 95% CI −42.6 to 11.6; P = 0.2616
Prabhakaran 2019 (1-year follow-up)	Self-reported adherence to antihypertensive drug on all 7 days prior to endline assessment	—	81.1%	1027	57.9%	1119	Risk difference[b] 23.1%, 95% CI 14.6 to 31.6%; P < 0.001
Choudhry 2018 (1-year follow-up)	Lipid-lowering medication: mean proportion of days covered over the 12 months after randomisation (prescription data)	—	48.2	1467	44.1	1503	Mean difference[a] 4.5, 95% CI 2.1 to 6.8 (P-value not reported)
	BP medication: mean proportion of days covered over the 12 months after randomisation (prescription data)	—	42.7	529	35.9	486	Mean difference[a] 8.5, 95% CI 5.4 to 11.7 (P-value not reported)
Márquez Contreras 2019 (1-year follow-up)	Proportion taking BP medication correctly on 80% - 100% of days (MEMS)	—	86.3%	73	62.7%	75	Risk difference[c] 21.6%, 95% CI −1.2 to 44.5; P = 0.064
McManus 2018 (1-year follow-up)	Mean adherence score for BP medication (MARS questionnaire score) (unclear what the score range is as applied in this report)	—	24.0	~ 327 (exact n unclear)	23.9	~ 348 (exact n unclear)	Adjusted mean difference 0.02, 95% CI −0.20 to 0.25; P = 0.833
Morillo-Verdugo 2018 (1-year follow-up)	Proportion adherent to 'concomitant medication'[d] - measured "with the Morisky-Green questionnaire and pharmacy dispensing records [....] patients were considered adherent [....] if they obtained a positive score"	—	87.7%	29	58.3%	24	Risk difference 27.9%, 95% CI 5.5 to 51.3

CI: confidence interval; SMS: short messaging service
[a]result reported in paper accounts for clustering.
[b]calculated using effective sample size (ICC: 0.05, average cluster size: 83).
[c]calculated using effective sample size (ICC:0.05, average cluster size: 37).
[d]various medications (see Characteristics of included studies for more detail).

APPENDICES

Appendix 1. Search strategies

MEDLINE (Ovid)

1 exp Cell Phones/

2 ((cell* or mobile) adj (phone* or telephon*)).tw.

3 (cellphone* or mobiles or smartphone*).tw.

4 ((mobile or handheld or hand-held or cell* or phone*) adj2 (device* or technolog* or app* or health*)).tw.

5 Text Messaging/

6 sms.tw.

7 ((text or short or multimedia or multi-media or mms) adj1 messag*).tw.

8 (texting* or texted or texter*).tw.

9 Telemedicine/

10 (mhealth or m-health or ehealth or e-health or telemedicine* or telehealth or telemonitor*).tw.

11 Reminder Systems/

12 (reminder* adj (text* or system* or messag*)).tw.

13 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12

14 exp Cardiovascular Diseases/

15 cardio*.tw.

16 cardia*.tw.

17 heart*.tw.

18 coronary*.tw.

19 angina*.tw.

20 ventric*.tw.

21 myocard*.tw.

22 pericard*.tw.

23 isch?em*.tw.

24 emboli*.tw.

25 arrhythmi*.tw.

26 thrombo*.tw.

27 atrial fibrillat*.tw.

28 tachycardi*.tw.

29 endocardi*.tw.

30 (sick adj sinus).tw.

31 hypertensi*.tw.

32 exp Hyperlipidemias/

33 hyperlipid*.tw.

34 hyperlip?emia*.tw.

35 hypercholesterol*.tw.

36 hypercholester?emia*.tw.

37 hyperlipoprotein?emia*.tw.

38 hypertriglycerid?emia*.tw.

39 arteriosclerosis.tw.

40 atherosclerosis.tw.

41 exp Cholesterol/

42 cholesterol.tw.

43 Blood Pressure/

44 ((high* or raise* or elevat* or heighten* or increas*) adj3 (blood adj2 pressure)).tw.

45 ((high* or raise* or elevat* or heighten* or increas*) adj3 (BP or DBP or SBP)).tw.

46 ((diastolic or systolic or pulse) adj pressure).tw.

47 exp Stroke/

48 (stroke or strokes).tw.

49 cerebrovasc*.tw.

50 cerebral vascular.tw.

51 apoplexy.tw.

52 ((brain* or cerebral or lacunar) adj2 infarct*).tw.

53 peripheral arter* disease*.tw.

54 aortic*.tw.

55 (arterial adj occlus*).tw.

56 infarct*.tw.

57 multiple risk factor.tw.

58 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57

59 randomized controlled trial.pt.

60 controlled clinical trial.pt.

61 randomized.ab.

62 placebo.ab.

63 clinical trials as topic.sh.

64 randomly.ab.

65 trial.ti.

66 59 or 60 or 61 or 62 or 63 or 64 or 65

67 exp animals/ not humans.sh.

68 66 not 67

69 13 and 58 and 68

CENTRAL

#1 MeSH descriptor: [Cell Phones] explode all trees

#2 ((cell* or mobile) near (phone* or telephon*))

#3 (cellphone* or mobiles or smartphone*)

#4 ((mobile or handheld or hand-held or cell* or phone*) near/2 (device* or technolog* or app* or health*))

#5 MeSH descriptor: [Text Messaging] this term only

#6 sms

#7 ((text or short or multimedia or multi-media or mms) near/1 messag*)

#8 (texting* or texted or texter*)

#9 MeSH descriptor: [Telemedicine] this term only

#10 (mhealth or m-health or ehealth or e-health or telemedicine* or telehealth or telemonitor*)

#11 MeSH descriptor: [Reminder Systems] this term only

#12 (reminder* near (text* or system* or messag*))

#13 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12

#14 MeSH descriptor: [Cardiovascular Diseases] explode all trees

#15 cardio*

#16 cardia*

#17 heart*

#18 coronary*

#19 angina*

#20 ventric*

#21 myocard*

#22 pericard*

#23 isch*em*

#24 emboli*

#25 arrhythmi*

#26 thrombo*

#27 atrial fibrillat*

#28 tachycardi*

#29 endocardi*

#30 (sick near sinus)

#31 hypertensi*

#32 MeSH descriptor: [Hyperlipidemias] explode all trees

#33 hyperlipid*

#34 hyperlip*emia*

#35 hypercholesterol*

#36 hypercholester*emia*

#37 hyperlipoprotein*emia*

#38 hypertriglycerid*emia*

#39 arteriosclerosis

#40 atherosclerosis

#41 MeSH descriptor: [Cholesterol] explode all trees

#42 cholesterol

#43 MeSH descriptor: [Blood Pressure] this term only

#44 ((high* or raise* or elevat* or heighten* or increas*) near/3 (blood near/2 pressure))

#45 ((high* or raise* or elevat* or heighten* or increas*) near/3 (BP or DBP or SBP))

#46 ((diastolic or systolic or pulse) near pressure)

#47 MeSH descriptor: [Stroke] explode all trees

#48 (stroke or strokes)

#49 cerebrovasc*

#50 cerebral vascular

#51 apoplexy

#52 ((brain* or cerebral or lacunar) near/2 infarct*)

#53 peripheral arter* disease*

#54 aortic*

#55 (arterial near occlus*)

#56 infarct*

#57 multiple risk factor

#58 #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57

#59 #13 and #58

Embase

1. exp mobile phone/

2. ((cell* or mobile) adj (phone* or telephon*)).tw.

3. (cellphone* or mobiles or smartphone*).tw.

4. ((mobile or handheld or hand-held or cell* or phone*) adj2 (device* or technolog* or app* or health*)).tw.

5. text messaging/

6. sms.tw.

7. ((text or short or multimedia or multi-media or mms) adj1 messag*).tw.

8. (texting* or texted or texter*).tw.

9. telemedicine/

10. (mhealth or m-health or ehealth or e-health or telemedicine* or telehealth or telemonitor*).tw.

11. reminder system/

12. (reminder* adj (text* or system* or messag*)).tw.

13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12

14. exp cardiovascular disease/

15. cardio*.tw.

16. cardia*.tw.

17. heart*.tw.

18. coronary*.tw.

19. angina*.tw.

20. ventric*.tw.

21. myocard*.tw.

22. pericard*.tw.

23. isch?em*.tw.

24. emboli*.tw.

25. arrhythmi*.tw.

26. thrombo*.tw.

27. atrial fibrillat*.tw.

28. tachycardi*.tw.

29. endocardi*.tw.

30. (sick adj sinus).tw.

31. hypertensi*.tw.

32. exp Hyperlipidemias/

33. hyperlipid*.tw.

34. hyperlip?emia*.tw.

35. hypercholesterol*.tw.

36. hypercholester?emia*.tw.

37. hyperlipoprotein?emia*.tw.

38. hypertriglycerid?emia*.tw.

39. arteriosclerosis.tw.

40. atherosclerosis.tw.

41. exp cholesterol/

42. cholesterol.tw.

43. blood pressure/

44. ((high* or raise* or elevat* or heighten* or increas*) adj3 (blood adj2 pressure)).tw.

45. ((high* or raise* or elevat* or heighten* or increas*) adj3 (BP or DBP or SBP)).tw.

46. ((diastolic or systolic or pulse) adj pressure).tw.

47. exp cerebrovascular accident/

48. (stroke or strokes).tw.

49. cerebrovasc*.tw.

50. cerebral vascular.tw.

51. apoplexy.tw.

52. ((brain* or cerebral or lacunar) adj2 infarct*).tw.

53. peripheral arter* disease*.tw.

54. aortic*.tw.

55. (arterial adj occlus*).tw.

56. infarct*.tw.

57. multiple risk factor.tw.

58. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57

59. random$.tw.

60. factorial$.tw.

61. crossover$.tw.

62. cross over$.tw.

63. cross-over$.tw.

64. placebo$.tw.

65. (doubl$ adj blind$).tw.

66. (singl$ adj blind$).tw.

67. assign$.tw.

68. allocat$.tw.

69. volunteer$.tw.

70. crossover procedure/

71. double blind procedure/

72. randomized controlled trial/

73. single blind procedure/

74. 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73

75. (animal/ or nonhuman/) not human/

76. 74 not 75

77. 13 and 58 and 76

CINAHL Plus

S71 S13 AND S58 AND S70

S70 S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69

S69 TX allocat* random*

S68 (MH "Quantitative Studies")

S67 (MH "Placebos")

S66 TX placebo*

S65 TX random* allocat*

S64 (MH "Random Assignment")

S63 TX randomi* control* trial*

S62 TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))

S61 TX clinic* n1 trial*

S60 PT Clinical trial

S58 S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57

S57 TI multiple risk factor or AB multiple risk factor

S56 TI infarct* or AB infarct*

S55 TI (arterial N0 occlus*) or AB (arterial N0 occlus*)

S54 TI aortic* or AB aortic*

S53 TI peripheral arter* disease* or AB peripheral arter* disease*

S52 TI ((brain* or cerebral or lacunar) N2 infarct*) or AB ((brain* or cerebral or lacunar) N2 infarct*)

S51 TI apoplexy or AB apoplexy

S50 TI cerebral vascular or AB cerebral vascular

S49 TI cerebrovasc* or AB cerebrovasc*

S48 TI (stroke or strokes) or AB (stroke or strokes)

S47 (MH "Stroke+")

S46 TI ((diastolic or systolic or pulse) N0 pressure) or AB ((diastolic or systolic or pulse) N0 pressure)

S45 TI ((high* or raise* or elevat* or heighten* or increas*) N3 (BP or DBP or SBP)) or AB ((high* or raise* or elevat* or heighten* or increas*) N3 (BP or DBP or SBP))

S44 TI ((high* or raise* or elevat* or heighten* or increas*) N3 (blood N2 pressure)) or AB ((high* or raise* or elevat* or heighten* or increas*) N3 (blood N2 pressure))

S43 (MH "Blood Pressure")

S42 TI cholesterol or AB cholesterol

S41 (MH "Cholesterol+")

S40 TI atherosclerosis or AB atherosclerosis

S39 TI arteriosclerosis or AB arteriosclerosis

S38 TI hypertriglycerid?emia* or AB hypertriglycerid?emia*

S37 TI hyperlipoprotein?emia* or AB hyperlipoprotein?emia*

S36 TI hypercholester?emia* or AB hypercholester?emia*

S35 TI hypercholesterol* or AB hypercholesterol*

S34 TI hyperlip?emia* or AB hyperlip?emia*

S33 TI hyperlipid* or AB hyperlipid*

S32 (MH "Hyperlipidemia+")

S31 TI hypertensi* or AB hypertensi*

S30 TI (sick N0 sinus) or AB (sick N0 sinus)

S29 TI endocardi* or AB endocardi*

S28 TI tachycardi* or AB tachycardi*

S27 TI atrial fibrillat* or AB atrial fibrillat*

S26 TI thrombo* or AB thrombo*

S25 TI arrhythmi* or AB arrhythmi*

S24 TI emboli* or AB emboli*

S23 TI isch?em* or AB isch?em*

S22 TI pericard* or AB pericard*

S21 TI myocard* or AB myocard*

S20 TI ventric* or AB ventric*

S19 TI angina* or AB angina*

S18 TI coronary* or AB coronary*

S17 TI heart* or AB heart*

S16 TI cardia* or AB cardia*

S15 TI cardio* or AB cardio*

S14 (MH "Cardiovascular Diseases+")

S13 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12

S12 TI (reminder* N0 (text* or system* or messag*)) or AB (reminder* N0 (text* or system* or messag*))

S11 (MH "Reminder Systems")

S10 TI (mhealth or m-health or ehealth or e-health or telemedicine* or telehealth or telemonitor*) or AB (mhealth or m-health or ehealth or e-health or telemedicine* or telehealth or telemonitor*)

S9 (MH "Telemedicine")

S8 TI (texting* or texted or texter*) or AB (texting* or texted or texter*)

S7 TI ((text or short or multimedia or multi-media or mms) N1 messag*) or AB ((text or short or multimedia or multi-media or mms) N1 messag*)

S6 TI sms or AB sms

S5 (MH "Text Messaging")

S4 TI ((mobile or handheld or hand-held or cell* or phone*) N2 (device* or technolog* or app* or health*)) or AB ((mobile or handheld or hand-held or cell* or phone*) N2 (device* or technolog* or app* or health*))

S3 TI (cellphone* or mobiles or smartphone*) or AB (cellphone* or mobiles or smartphone*)

S2 TI ((cell* or mobile) N0 (phone* or telephon*)) or AB ((cell* or mobile) N0 (phone* or telephon*))

S1 (MH "Cellular Phone+")

Conference Proceedings Citation Index-Science (CPCI-S)

23 #22 AND #21 AND #8

22 TS=(random* or blind* or allocat* or assign* or trial* or placebo* or crossover* or cross-over*)

21 #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9

20 TS=(arterial near occlus*)

19 TS=(aortic* or infarct* or multiple risk factor)

18 TS=peripheral arter* disease*

17 TS=((brain* or cerebral or lacunar) near/2 infarct*)

16 TS=(cerebrovasc* or cerebral vascular or apoplexy)

15 TS=(stroke or strokes)

14 TS=((diastolic or systolic or pulse) near pressure)

13 TS=((high* or raise* or elevat* or heighten* or increas*) near/3 (BP or DBP or SBP))

12 TS=((high* or raise* or elevat* or heighten* or increas*) near/3 (blood near/2 pressure))

11 TS=(hypertensi* or hyperlipid* or hyperlip?emia* or hypercholesterol* or hypercholester?emia* or hyperlipoprotein?emia* or hypertriglycerid?emia* or arteriosclerosis or atherosclerosis or cholesterol)

10 TS=(sick near sinus)

9 TS=(cardio* or cardia* or heart* or coronary* or angina* or ventric* or myocard* or pericard* or isch?em* or emboli* or arrhythmi* or thrombo* or atrial fibrillat* or tachycardi* or endocardi*)

8 #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1

7 TS=(reminder* near (text* or system* or messag*))

6 TS=(mhealth or m-health or ehealth or e-health or telemedicine* or telehealth or telemonitor*)

5 TS=(sms or texting* or texted or texter*)

4 TS=((text or short or multimedia or multi-media or mms) near/1 messag*)

3 TS=((mobile or handheld or hand-held or cell* or phone*) near/2 (device* or technolog* or app* or health*))

2 TS=(cellphone* or mobiles or smartphone*)

1 TS=((cell* or mobile) near (phone* or telephon*))

ClinicalTrials.gov

Condition or disease: CVD OR “blood pressure” OR cholesterol

Other terms: “mobile phone” “medication”

Study type: Interventional Studies (Clinical Trials)

WHO International Clinical Trials Registry Platform (ICTRP)

Condition: CVD OR “blood pressure” OR cholesterol

AND

Intervention: “mobile phone”

WHAT'S NEW

Date	Event	Description
31 March 2021	Amended	Minor correction in abstract.

HISTORY

Protocol first published: Issue 5, 2017
Review first published: Issue 6, 2018

Date	Event	Description
7 January 2021	New search has been performed	Review updated with a search on 7 January 2020; 10 new trials included and top-up search on 8 January 2021 with 18 potentially eligible studies added to 'Studies awaiting classification'.
8 October 2020	New citation required but conclusions have not changed	The update has not changed the conclusions of this review.

CONTRIBUTIONS OF AUTHORS

MP: registered the title with the Cochrane Heart Group and prepared the first draft of this review update.

KM: contributed to screening studies, data extraction, and writing the review update.

SW: contributed data extraction and writing the review update.

SR: contributed to data extraction and writing the review update.

AG: contributed to screening studies and writing the review update.

SB: contributed to designing and writing the review update.

PP: contributed to designing and writing the review update.

CF: conceived the idea for this review, led on designing the protocol and contributed to writing the review update.

DECLARATIONS OF INTEREST

MP: none known.

SB: none known.

PP: none known.

CF: none known.

SW: none known.

KM: none known.

AG: none known.

SR: none known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- NIHR, UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In our protocol, we specified how we would deal with trials that included a mix of participants meeting the criteria of primary prevention and secondary prevention of CVD, stating: "where we identify trials that include a subset of eligible participants, we will contact the authors to request data for only those participants of interest. In the event that we are unable to access these data, we will apply a cut-off whereby only trials in which at least 75% of participants meet the criteria for primary prevention will be included."

However, we did not specify how we would deal with trials that included a mix of participants who were prescribed CVD prevention medication and participants who were not prescribed CVD medication. Given that we stated we would include trials of interventions that target medication adherence alongside other lifestyle modifications, some of our trials identified for inclusion in this review included participants who had and participants who had not been prescribed CVD prevention medication. We extracted primary outcome data of objective measures of medication adherence (e.g. blood pressure, low-density lipoprotein cholesterol, etc.) for these mixed populations.

We stated that we would extract low-density lipoprotein cholesterol as an objective indicator of adherence to lipid-lowering medication. In addition, we have also extracted total cholesterol and high-density lipoprotein cholesterol.

We stated we would report dichotomous outcomes as risk ratios. However we report them as odds ratios in order to allow for extraction of appropriately-adjusted results and comparability across effect estimates.

In the update of this review we made the following changes. We assessed risks of bias separately for objective outcomes, e.g. blood pressure, and self-reported subjective outcomes, e.g. self-reported adherence. This meant that for the overall study assessment, we categorised a trial as being at low risk of bias if it was rated as low risk in all domains, with the exception of blinding of participants and personnel *and* blinding of self-reported outcome assessment.

We did not assess the behaviour-change techniques in interventions, as we did not have the resources, and this was not considered to add materially to the value of the prior version of the review. Subgroup analyses would not therefore have been carried out on this basis had we conducted them. We did not request that authors provide us with disaggregated data only for those who met criteria for primary prevention or who were on CVD medication, or both. This was because in the previous version of the review this did not result in any data-sharing. Instead we contacted authors to clarify the proportion of participants meeting primary-prevention criteria, and the proportion prescribed CVD medication, when this had not been stated in the study report.

INDEX TERMS

Medical Subject Headings (MeSH)

Bias; Blood Pressure; Cardiovascular Diseases [*prevention & control]; *Cell Phone; Cholesterol, LDL [blood]; *Medication Adherence; Primary Prevention [*methods]; Randomized Controlled Trials as Topic; *Text Messaging

MeSH check words

Adult; Humans